

## Calling the Odds for the Cancer Sweepstakes

THE competition between the United States Administration and its political opponents to offer American taxpayers the glossiest prospectus for the cure of cancer is not merely potentially damaging for the balance of scientific work in the United States but a bad precedent for the future and a bad example for the rest of the world (see page 414). It is therefore important that everybody concerned should understand how this macabre competition has arisen and where it could, with bad luck, end. The immediate issue is whether federal support for cancer research should be channelled through the National Cancer Institute, one of the several institutes contained within the loose federation called the National Institutes of Health, or whether there should be set up a grander organization with the status of a bureau within the Department of Health, Education and Welfare. For several years, the National Cancer Institute has been one of the best endowed of all the members of the NIH. In the current financial year, the institute's budget has been increased by \$50 million, and it would have an extra \$30 million to spend in the coming year if Congressional committees have their way.

Up to a point, this sudden largesse is at once timely and appropriate. There is enough promise in the state of research in the past few months, which demonstrated a connexion between viruses and carcinogenesis, for those working in the field to look forward to rapid progress in the understanding of at least some form of the disease. Given that understanding is often the first step towards better treatment, and the cruelty of the toll which cancer takes among western populations, this is a sensible direction in which to change the pattern of scientific research in the United States. To be sure, there can be no assurance that there will be enough skilled researchers with sufficiently good ideas for the extra money to be well spent. Cancer research has a long and discreditable history of too much money chasing too few ideas. But there is at least a chance that some benefit will eventually accrue from the extra money. There is, however, nothing in the developments of the past few months to sustain the belief that the current interest and promise of research will lead to methods of curing cancer in any form in the foreseeable future. It is merely that there may be a chance that this will happen. It is true that neither the Administration nor its critics in Washington have made specific promises that extra money spent now will cure cancer (whatever that phrase may mean) within the decade, but their protestations of zeal on behalf of cancer research are implicitly becoming promises that something definite will happen. The same tendency has even afflicted Britain, where the Cancer Research Campaign is now raising money with the slogan "Conquer Cancer in the Seventies". If the disease is cruel, so too is the disappointment that comes from too eager an interpretation of the promise of recent research. What politicians and the

scientific community should together be concerned to establish is an accurate public appreciation of the distinction which must be made between research, however promising, and methods of treatment.

If, in the United States, all parties have somehow avoided explicit and overdefinite promises of cure, it seems to have been established as a convention of political warfare that spending money on cancer research or other acts which may be considered as solicitude for cancer researchers will be interpreted as solicitude for those who are likely to die of cancer and for their relatives. The proposal that the National Cancer Institute should be separated from the NIH, originally put forward by Senator Edward Kennedy and now taken up by the Administration, is such a move. In exactly the spirit in which governments occasionally attempt to advertise their concern for some problem or another by appointing an excessively senior or distinguished person to take charge of it, the designation of the National Cancer Institute as something standing on its own feet is intended as a demonstration of the importance attached to the whole field. One obvious danger is that such a separation of cancer research from other kinds of research, especially if the first is excessively well endowed, will stultify and not fructify the work. There is a host of chilling examples to bear out this assertion. But it is also entirely possible that the arrangements now proposed contain within themselves the seeds of disappointment. After all, was not NASA set up ten years ago with the intention of reaping what was alleged to be the rich harvest of applied space research? Those who are at present set on the concept of an ever grander institution for federally supported cancer research should try to anticipate the problems there will be if, for some reason which cannot be anticipated at this stage, Congress turns sour.

If the proposals on which the Administration and Senator Kennedy appear to have compromised are likely to be bad for cancer research as such, they will also have unhappy consequences elsewhere. For one thing, singling out one of the National Institutes of Health for special treatment is by itself an unhappy precedent which is likely to undermine the loose but apparently congenial federation of Bethesda. Will the National Heart and Lung Institute be the next to make a break for status and autonomy? Or will the dental surgeons of the United States and their supporters somehow find a way of putting pressure on the Administration so as to make the National Institute of Dental Research (one eighth of the size of the National Cancer Institute but quickly growing) into an independent entity? Is it not even a slur on dentists, let alone on those who brush their teeth twice a day, that dental science should be the responsibility of an institute which lacks the degree of autonomy now likely to be synonymous with self-respect? By arguments like these, there is now a serious danger that the integrity and the



success of the National Institutes of Health will be seriously undermined. That is a practical issue which the Administration and Senator Kennedy should both consider seriously.

Another shadow cast by what is happening in Washington is more distant but in the long run more worrying. One of the accusations against professional science in the past few years has been that it is prone to mistake means for objectives. There is a stream of public complaint at projects as diverse as the journey to the Moon and the design of supersonic transport aircraft that they are more necessary to the enjoyment of the scientific community than to their potential users. There is a danger that the

care now being lavished on the cancer programme in the United States will similarly be recognized as an occasion when, for apparently beneficent motives, the scientific community is prepared to spend money in large quantities without asking whether it can spend it wisely. It is possible that the tussle between the Administration and Senator Kennedy has hidden from public view careful studies of the kind now familiar when individual scientists find themselves asking for help from grant-giving bodies, but the chances are that everybody is being carried along by enthusiasm and wishful thinking. There is plenty of experience in the years since the Second World War to show how disastrous that can be.

## How the British Association May Survive

THE British Association, traditionally too sensitive about its public reputation, should regard the interest which outsiders take in its affairs not as criticism but as a mark of affection. The proposals for reform put forward by the Committee of Review are of great interest not merely to members of the association but because they could provide a framework within which the discussion of public issues arising from science and technology could be conducted. For the committee is right to have accepted the view that there is an urgent and continuing need in Britain for an informed platform for the discussion of issues as different as the proper balance of scientific education in the schools and universities, the planning of scientific research in an economic environment which is increasingly idiosyncratic and difficult and the application of scientific techniques to the moderation of pollution and the other untoward side effects of scientific industry. The irony in the British Association's fortunes brought out by the recommendations of the Committee of Review is not merely that exactly the same role was urged on the association fifteen years ago, at a point in its history which also seemed as critical as the present, but that in the nineteenth century and much more recently, the association has had a distinguished record of intervention in important debates on issues where science and technology are closely concerned. Thus the British Association helped to awaken public interest in Britain in the relationship between scientific research and industrial prosperity by the publication in the mid-fifties of a careful study by C. F. Carter and B. L. Williams (now respectively the vice-chancellors of the Universities of Lancaster and Sydney). Although there may be some members of the Association who will find it hard to accept all the changes now urged upon them, the notion that there should be a more active and deliberate intervention in public debate is by no means an outrageous innovation but, rather, a return to past tradition.

But what in present circumstances is to be done? The fashion which now grips the prosperous west for public anxiety about the consequences of science and technology cannot be ignored. It is plain, however, that there are serious dangers in too slavish an acceptance of the popular view that pollution is to the twentieth century what sin was to the twelfth century—too many reputations have been lost already for a reinvigorated British Association to take such a risk. But what may be called the environmental issue cannot be shirked. Is there not an urgent need, for

example, for some of the hard-headed economic studies that will help people to decide when the banishment of pollution may be an advantage to a population, or a prudent way in which to spend resources, and when the fight against pollution is merely an economic waste? It would also help a proper public appreciation of the place of science and technology in the modern world if a body such as the British Association were able to inform the debate about the ethics of medical research, for example, with a sensitive appraisal of the steps which should be taken to regulate these activities but not to stifle them. But there are also important issues within the scientific and technical professions which need to be better understood and argued. In the development of the university curriculum, scientists need better advocacy and fuller debate than they have enjoyed so far. There are questions about the relationship between research and universities which should be argued out. It is also inevitable that if the British Association seizes the opportunity with which it is presented, there will have to be a serious examination of some of the points which the sociologists are constantly raising—is there, for example, an inherent inconsistency between the expressed humanitarian goals of scientists and the ways in which the profession of science is organized? No reputations need be put in hazard by a serious study of questions like these. Not merely the British Association but the British public would benefit if the job were done well.

So will the membership agree? In circumstances like these, it is easier to applaud reform than to accept change and the most obvious danger now is that the management of the association will find itself instructed to carry out its new tasks but denied the smoother organization that is a prerequisite for success. The difficulty, of course, is that the association has inherited with its traditions a range of activities which cannot easily be run in harness. The Annual Meeting, which gives great pleasure to those who attend it, is necessarily much less like a learned society's meeting than an intellectual holiday camp (which is no disgrace). It serves not merely as a means by which scientifically inclined people can be brought up to date in a comparatively uncompetitive way, but also as a means of drawing attention to the association's public work. One difficulty is that those who at present attend the Annual Meeting are often quite properly indifferent to the causes which the association is now enjoined to follow. The ideal, of course, is that there should be some device for



combining the best parts of the traditional meetings with the public platform which will be needed for the proper presentation of the association's interests in public issues. It could well turn out that the ideal is unattainable because

it costs too much, in which case it is to be hoped that the association's members will acknowledge that it is better to make a dash for survival at this stage than to face the prospect of a slow but inevitable decline.

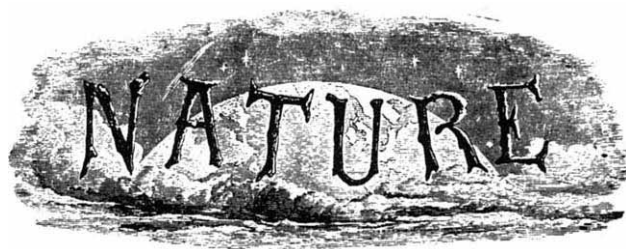
## Geographers as Authors

THE idea that geographers, of all people, should need instruction in how to write will no doubt be a surprise to many geographers, let alone to their colleagues in other fields, and for that reason it is creditable that Mr T. W. Freeman, Reader in Economic Geography at the University of Manchester, should have been able to write a book, *The Writing of Geography* (Manchester University Press, £0.84), which is neither patronizing nor platitudinous. To be sure, books which are bound to contain lots of examples of how other people write badly and which nevertheless avoid rubbing salt into open wounds are entertaining to read, and those who are not geographers can cluck their tongues and say to themselves that such practices would never be allowed in, say, chemistry or physics. . . . Mr Freeman has advice for everybody, however. He opens by urging that writers should begin by making sure that they have a rounded view of what they want to write about, even if this implies that they must take extra care to collect enough information. He goes on to argue that research and authorship are inseparable parts of scholarship—a person should write up an account of his work as he does it, not merely because he may otherwise forget what he has to say but because the act of writing is a stimulant to further thought. And, in the best traditions of Gowers and Fowler, Mr Freeman has good sport with the unnamed authors of solecisms such as “the rapidly developing shipyards added to the number of workers”. Relenting, he commends vivid writing such as “To be poor, in West Indian eyes, is to be black; to be white is to be rich; and to be coloured is to be somewhere in between, relatively well-off, middle-class”. All this is good knockabout stuff, but it is too bland. Academic prose is much worse than Mr Freeman implies. That it should remain so is a continuing scandal.

The empirical evidence that scholars in general and scientists in particular should write plainer English is plentiful; most journals are full of it. The most serious complaint is not at the way in which people use words but at their motives in writing at all. Good grammar is only a means to an end and there is no reason why some authors should not be able to convey the essence of what they have to say by methods that would bring a rap over the knuckles in many Victorian primary schools. It is true, of course, that a writer needs to be sure of himself before he throws the grammar book away but what he most of all needs on his side is a direct appreciation of why he wants to write. It must be acknowledged that in a good deal of what academics write, objectives are unclear or, worse, suspect. Sometimes, articles in journals seem to have been written with the intention not of communicating to readers news of some development of interest to them as well as to the author, but of creating the impression that something is going on without revealing what this may actually be. These are the articles which are written for posterity (when some ambiguously constructed phrase may be reinterpreted as

the first hint of an important discovery) or for immediate colleagues and competitors (who may have the information necessary to interpret what the author has written). On other occasions, the exposition is clear enough but is also so dry that it will serve only as a statement of facts, not as a means of persuading readers to take as their own ideas or points of view which may not previously have occurred to them. In short, a common fault in academic writing is that it is cryptic (which is an offence against scholarship) or unpersuasive (which is a way of making sure that it serves no purpose). Over the years, the convention has been established, especially in the sciences (which include geography) that just as data are in themselves neutral, so scientific records should be neutral—raw material with which readers must make up their own minds. One obvious difficulty is that most readers are never able to appreciate the neutral data as sensitively as the author, with the result that they often miss the point. A more serious flaw in this view of how the scientific literature should be written is that attempts by authors to conceal the views they wish their readers to adopt lead them into tortuous arguments which either bemuse their readers or, worse still, mislead them.

## 100 Years Ago



WE reprint the following sentence from the recently published address of the President of the Tyneside Naturalists' Field Club, commending it to the notice of similar institutions throughout the country now that the season for excursions is commencing:—“We have no law excluding ladies from our club, but yet we have no lady members. Ladies, however, sometimes attend our meetings, and it would, I think, be an advantage to the club (may I hint also that it might be an advantage to the ladies?) if more of them came, and oftener. It is of infinite importance that mothers should be able to impart to their children an intelligent interest in Nature. They cannot do this unless they first possess that interest themselves, and in what way can it be more pleasantly developed and refreshed than by meetings such as ours? It may perhaps be objected that the length and occasionally the rugged character of our walks prove an obstacle to the presence of the weaker sex; but my impression is that this is not the case to any very serious extent, and in many of our excursions ladies have proved themselves quite equal to walks as long and as arduous as are at all desirable for our purposes. I would therefore recommend—not any new rule, which is needless—but simply that we should persuade our lady friends to join the club as members, and not as only casual visitors.”

From *Nature*, 4, 149, June 22, 1871

## OLD WORLD

### EXPERIMENTS ON ANIMALS

## Report Debated at Last

THE House of Commons last week resolved "to take note of the Report of the Littlewood Committee on Experiments on Animals". As over six years have elapsed since the late Sir Sydney Littlewood presented his report to Parliament, this was surely the very least expected of the House. Yet in opening the debate on the report, the Under Secretary for State for the Home Department, Mr Mark Carlisle, observed that "The Government have not yet finalized their attitude to the report in the sense of assuming a commitment to legislate".

The debate, a commendably objective affair free from unwarranted calls on the emotions, centred around three chief issues. As experiments on living animals seem necessary and inevitable, how are these to be limited and controlled? Are there feasible alternatives to the use of living animals for medical research? And how relevant are the six year old recommendations of the Littlewood committee to the present (and future) situation? What emerged was a prospect of more investigation before legislation and a suggestion that commercial interests may be charged for their experimenter's licences to subsidize the watch kept on their operations.

Mr Carlisle said that the Home Secretary recognized the key role of the ministry's inspectorate in checking that the existing legislation for animal experiments is observed. He showed that in 1963, when the Littlewood report was commissioned, there were 5,932 people licensed to carry out experiments on living animals and only six inspectors. By 1965, the strength of the inspectorate had risen to eight, but the number of licensees had increased to 7,053. By 1969 there were 9,252 active licensees marshalled by thirteen inspectors, or about 712 licensees to each inspector. The present inspectorate includes a chief inspector, two superintendent inspectors and five inspectors with veterinary qualifications. Mr Carlisle accepted, however, that their number is still eight short of the strength recommended in the report, but that "the ratio is such that the inspectors are carrying out their work adequately", a view which Mr F. A. Burden felt was "either very optimistic or very foolish". If funds were the obstacle, said Mr Burden in rejoinder to Mr Carlisle's claim that it was not a shortage of qualified people which prevented further appointments, then perhaps a charge might be made for

licences awarded to commercial undertakings, an idea which Mr Carlisle said he would bear in mind. Mr Kenneth Lomas, who has pressed the Government to establish an institute to examine methods of medical research which do not involve living animals (see *Nature*, **230**, 347; 1971), suggested that the number of licensees is nearer 14,000 than 9,000. Carlisle agreed but explained his figure included only those operators which the experimental returns showed to be active.

In 1964, the total number of experiments reported was 4.49 millions. There were 4.61 millions in 1966, and the estimated total for 1970 is 5.65 millions. Seventy per cent of these experiments involve mice, fifteen per cent rats and ten per cent guinea-pigs. All other species combined make up the other five per cent. These figures include all experiments involving "disease, discomfort or disturbance of normal health". In other words, the experiment need not necessarily mean pain to the animal. Furthermore, each animal used in an experiment counts as one experiment. Mr Carlisle observed that the Littlewood report, from evidence obtained in 1963-65, found that "the risk of unnecessary repetition of experiment is small" and that there "is no evidence of serious wastage of animals in recent years".

Mr Elystan Morgan, while paying tribute to the merit of the Cruelty to Animals Act of 1876, which sets the conditions in which experiments may be performed on living animals in England and Wales, felt that new legislation is called for after 95 years. New developments in medical and biological research require fresh regulations. Of the 83 recommendations in the report, 48 would require legislation. Mr Burden took up the question of the Advisory Committee, the body which advises the Ministry on the administration of the 1876 Act. Why, he wanted to know, has the committee decreased in number from 11 in 1965 to 9 in 1969? Does the committee serve no useful purpose? How many times a year does the committee advise the Ministry, and what are the nature of its recommendations? Mr Carlisle said that the only difficulties found in filling the committee's ranks were administrative ones. The committee had been consulted every year since 1963 except for 1969. Twelve cases had been referred to the committee between 1964 and 1968, and nine of these experiments had been allowed.

Almost as much time during the debate was given to soul searching over the delay in bringing the report before the House as to the recommendations of the report itself. Mr Richard Body detected a sense of unreality in the debate because of two

changes since the report was published: the increase in the number of animals used annually, and advances in alternative means of research. Mr Carlisle agreed that many factors could have altered since 1965 and that "a further review might be necessary if legislation were to follow". On the question of alternative methods of research, Mr Carlisle said that this was a matter purely for the Department of Education and Science, and that the Medical Research Council view is that "the use of animals remains essential for the advancement of medical and biological research".

Mr Carlisle could offer no solution to the three unanswered questions which lie at the heart of the Littlewood report: Who can say if satisfactory alternative tests might not be developed if certain animal experiments were banned? Who is to say if medical research, with its emphasis on animal experiments, is on the right road? And who takes responsibility for the ethical judgment to use animals for experimental purposes? He thought that a legislative response to these questions would require "a tremendous act of faith or a comprehensive Measure providing for evaluation and direction of all biological and scientific research".

### MAGNET RESEARCH

## Higher Fields for Oxford

WITH a typically British combination of the old and the new, the Science Research Council is about to take a cautious step forward in the field of ultra-high magnetism by providing the funds (£79,000) for a 16 Tesla (160 kG) magnet to be built over the next year at the Clarendon laboratory. So far, the Oxford group has been able to utilize steady fields of up to 11 T in its experiments on the electrical properties of semi-conducting and insulating materials and in work on the magnetic ordering of solids. For one brief moment, a machine at the Royal Radar Establishment (RRE) recently achieved a field of 17.8 T, and this same machine can produce reasonably steady fields of 15 T regularly, as can comparable systems in other European laboratories. But the achievement of a steady 16 T field in an experimental chamber 5 cm in diameter will certainly represent a small step forward.

The nature of the hybrid machine planned does to some extent limit the field obtainable. A new superconducting magnet using the latest materials and techniques will be constructed, and this alone should produce a very steady field of 7 T in a bore 24 cm in diameter. The old part of the equipment, a copper solenoid powered by the



Clarendon's existing 2 MW DC motor-generator, will fit inside the new magnet, and bring the total field in a central experimental region 5 cm across up to 16 T.

This generator is very old indeed, having started its life 60 years ago as the power supply for Manchester's trams. But in this kind of work, reliability is as vital as other aspects of the performance of the machine, as demonstrated by the unfortunate breakdown of the RRE machine when pushed beyond its normal limits. There is also a point at which it becomes increasingly difficult to achieve even the smallest further step. More powerful machines require more stringent safety precautions, and the field increases only as the square root of the power supplied, so that both financial and technical problems are becoming almost insuperable above 15 T. At MIT, for example, where the only hybrid of this kind yet under construction is planned to have an eventual operating capacity of 22.5 T, the 50 per cent increase in field will be achieved using an 8 MW generator—that is, with four times more power than the Clarendon generator—and the added cost of effective fail-safe precautions has become a significant factor in completing the machine, although no exact figures concerning this aspect of the budget have been released.

Although this cannot be said to represent a giant leap for mankind, there are circumstances in which a leap into the unknown is an undesirable risk. There will certainly be many scientists both in the United Kingdom and from elsewhere glad to make use of the 16 T machine under the visiting facilities which the SRC will undoubtedly offer.

#### CHEMISTRY AND INDUSTRY

### Society Reorganizes

THE Society of Chemical Industry, whose aims are to further applied chemistry and encourage improvements within the chemical industry, has now shown a deficit for the second year running on its income and expenditure account. But the society seems to be confident that new investment and publishing policies will radically alter the situation by 1972. Most of the deficit—£30,296 in 1970, compared with an income of £251,000—can be explained by heavy losses on publishing, the steady increase of administrative expenses, and a drop in income from investments. Furthermore, the membership is dwindling; the society numbered about 7,000 ten years ago, but now has a membership of less than 6,000, which is falling at the rate of almost one hundred annually.

In 1969, the writing was really on the wall, and it was becoming clear that serious measures would have to be taken to reverse the sorry trend in the society's fortunes. There seemed to be a natural place for the society in the linkup of other chemical societies which was under discussion at the time (see *Nature* 228, 597; 1970) and there is no doubt that the Society of Chemical Industry would have made a fitting backbone to the industrial division of the new amalgamation which is already functioning, even though it does not come into existence formally until January 1972.

The referendum on the proposed merger which the society held in July 1970 was by no means conclusive, and of the 54 per cent of the membership who voted, only 68.3 per cent were in favour of taking part in the merger on the terms then available; it was certainly very doubtful in law whether a chartered body could commit itself to a merger with the agreement of such a small proportion of the membership, and indeed several members of the Society of Chemical Industry apparently intended at the time to press this legal point if plans for the merger went ahead. The Royal Institute of Chemistry was also making clear during the summer of 1970 its intention to interest itself much more in the salaries and conditions of employment of its members. At about the same time, Mr Leslie Williams, then President of the Royal Institute of Chemistry, referred to possible moves in the future towards a body operating under only one charter, and said that the quite considerable number of members of the Chemical Society who chose not to be members of the institute would "constitute the main barrier in the way of taking amalgamation to its logical and desirable end, that of one chartered organization" (*Chemistry in Britain*, 6, 300; 1970). This and other policy statements by the institute towards the end of 1970 seem to have alarmed the Society for Chemical Industry, which saw itself becoming subservient or even disappearing altogether.

The Society of Chemical Industry now seems reconciled to lone existence, and Mr George Beeby, the President of the Society for Chemical Industry, has described the amalgamation of a learned body with a professional body as "unnatural". Of course it is easy to level the familiar criticism that the Society of Chemical Industry is really something of a club for senior managers from the chemical industry, and is therefore not particularly interested in the trade union aspect of the new Chemical Society, but the fact of the matter is that almost 25 per cent of its membership of 6,000 are not chemists.

One particular advantage that would have accrued to the Society of Chemical Industry if it had joined the new Chemical Society is that it would then have had access to their publishing facilities, which already have a turnover of about £1 million per year. In the circumstances, however, the society now has to look seriously at the steps which must be taken if it is to remain a viable, independent body providing something of value to its members. Certainly the society's future plans for its publications—which include its house journal *Chemistry and Industry*, sent to 4,000 subscribers as well as to all the members of the society—and five other journals with circulations up to 3,000, are wide ranging. *Chemistry and Industry*, for example, is to be published twice a month instead of weekly after January 1972, and agreement has been reached with a commercial publisher, who will eventually publish and promote all the journals on behalf of the society. In the past, the society has simply not been geared to maximizing the sales of its journals and advertising revenue has suffered as a consequence. The secretary of the society, Dr D. H. Sharp, is confident that these changes will be a success.

The society is, however, not relying entirely on the prospect of better things to come. For example, it owns fairly long leases on extensive property in Belgrave Square, and these premises are not at present used to best advantage. The membership subscription is unlikely to be increased from £6 a year because of competition from the industrial division of the Chemical Society, which has an annual subscription of only £2.10. Luckily, there is a nest-egg of about £32,000 that may cushion the society against further trouble, even without breaking into the trust funds.

#### METEOROLOGY

### GARP'S Gamp Unfurls

Now that the World Meteorological Organization and the International Council of Scientific Unions have set their seal of approval on the tropical weather experiment in the Global Atmospheric Research Programme, it remains only to be seen if GARP's planning committee can muster enough support from the participating nations to ensure success. The chief aim of the experiment, scheduled for 1974, is to gather information about the formation, structure and properties of tropical cloud clusters. These clusters, which in equatorial regions can stretch for 500 miles, hold the key to the movement of heat and moisture from tropical oceans upwards and towards the poles to feed the Earth's major wind systems.

Numerical information about this interaction between air and sea is urgently needed to check the accuracy of present mathematical models of the world's weather and to form the basis for better ones in the future.

The tropical experiment will be the first major project which GARP will have undertaken since its formation as a reply to President Kennedy's call to the UN in 1961 for more and better weather-watching. The plan is to co-ordinate an international fleet of research vessels, specially equipped aircraft and weather satellites in and about 1000 square kilometres of the Eastern Atlantic Ocean. For three months, the area will be under continual surveillance by sea, air, and space, and a coherent picture should show the life history of a cloud cluster.

Finance for the experiment will be derived partly from the nations taking part, and partly from WMO funds. The sum required will be large, but limited funds were made available by the WMO this April to establish and maintain a small planning group. This unit, which includes Dr J. P. Kuettner of the United States, and Dr N. E. Rider from the United Kingdom, takes responsibility for marshalling and co-ordinating the research teams and equipment from the participating countries. Dr Kuettner was director of BOMEX, a project similar to the GARP experiment, but on a smaller scale, which the US mounted in the Barbados area in 1969.

The British contribution to the experiment, two research ships and one aircraft apart, will be to provide a

headquarters for the planning team at the Meteorological Office, Bracknell, Berkshire. The US and USSR were ruled out as hosts for diplomatic reasons, and at Bracknell there is now one of the largest computers in Europe, an IBM system 360 model 195, which will be used to process and digest the vast quantity of data which should emerge from the experiment.

The chief problem will be to weld the respective efforts of the six or seven participating nations into a cohesive whole. In particular, all the data must be compatible for maximum benefit to be reaped from the study. The experience of the International Geophysical Year, which left a trail of uncollated data in its wake, should ensure that the GARP planners make no such mistake.

## British Association Committee of Review Reports

THE British Association appears finally to have decided on a course to pursue in the years immediately ahead. After brooding on the subject since last October, the Committee of Review set up after the annual meeting at Durham last year to consider future policies and methods of organization has put forward a set of recommendations which are at once constructive and radical. It remains to be seen how successful the council of the association will be at championing the causes which the Committee of Review has spelled out. At the next annual meeting of the association at Swansea from September 1 to 8, the ultimate decision rests with the General Committee of the British Association, an uncounted body of people consisting of past and present members of the council, past and present presidents of the sixteen sections of the British Association, vice-presidents and secretaries of the sections, retired recorders and numerous other people nominated by the council. One of the hurdles yet to be surmounted will no doubt be that a part of the new plan for the British Association is that the General Committee, whatever it may be, should delegate its powers to a small reconstituted council, which is actually to be elected by the membership of the association.

If the new proposals are accepted by the British Association as a whole, one result will be that the association is much more closely involved than in the recent past with public issues. In a statement issued this week, the associa-

tion says that it has "an important role for the future in stimulating public interest in science and technology, in the relation of science and technology to social problems and in promoting the advance of science and technology to the benefit of the community". This is apparently intended to be a declaration that the association will graft on to its present activities a programme of seminars and study groups designed so as to illuminate issues in science and technology of public importance.

To the extent that declarations of intent may be held to presage policies, this part of the new plan should go a long way to meet the criticisms from members of the British Society for Social Responsibility in Science who, at the Durham meeting last September, argued that the British Association was socially almost unresponsive. In the recent brooding over the association's future, one of the unexpected parts of recent history to have come to light is that a committee under Sir Ben Lockspeiser, faced with almost identical problems to those considered by the new Committee of Review, advocated in 1957 that there should be a programme of intellectual work in between annual meetings intended to study "specific problems relating to the impact of science on society" and public conferences on "subjects of immediate national or public importance". Plainly there are plenty of opportunities for slips between the cup and the lip.

In practical terms, what the Committee of Review seems to have advo-

cated is a programme of symposia and public meetings to be held in between the annual meetings which are the association's most conspicuous claim on public attention. First, there would be an attempt to provide a forum for discussions of matters of public interest, from pollution to the planning of university research. At the same time, the committee is thought to have advocated the carrying out of studies on particular issues which would lead to detailed and authoritative reports which would themselves form part of a deliberate publications programme. Plainly the Committee of Review is hoping that this device will help in a modest way to increase the association's income.

From the statement issued this week, the Committee of Review is plainly hoping that the torrent of talk that it seeks to encourage at the centre will be echoed up and down the length of Britain by local discussions, presumably organized by the area committees of the British Association which have been strengthened in the past few years and which are at present the chief vehicles for the association's work with local education authorities. For this and other reasons, the Committee of Review has urged that there should be a more generous (but still modest) subvention of the area committees in the years ahead.

The reorganization of the Annual Meeting is plainly a much more contentious matter, and this is one of the points on which some of the strongest opposition to the review proposals is



likely to be concentrated. Legend has it that the tradition of beginning each Annual Meeting on a Wednesday and allowing it to last for the whole of a week goes back to the days when many of the association's members were country parsons who could fill their pulpits with a locum for one Sunday but who were reluctant to be away for two Sundays in a row. The effect of this strange pattern seems, however, to have become more a discouragement than an incentive to attendance at the Annual Meeting. Although attendance at the Annual Meeting has fallen below 2,000 only in the past two years, the number of fully paid-up members who stay the whole week's course (and who pay for the privilege of doing so) is thought to be only a few hundred. Many of the several hundred people who speak each year at the Annual Meeting tend to arrive by one train and depart on the next.

The Committee of Review has advocated Annual Meetings which are "shorter and simpler". It wants to see less specialist material and more about the public implications of science and technology. One immediate change is that the meeting in Leicester in 1972 will run from Monday to Saturday, but this choice seems to have been forced on the association as much by the difficulties of arranging for a different timetable at Leicester as by pure logic or even a knowledge of what members need. In its advocacy of a simpler and more flexible pattern for the Annual Meeting, the Committee of Review does, however, say explicitly that in future years London should occasionally be chosen as a venue. In the belief that it has been the association's task to carry the scientific message into the country, cities outside London have been chosen for the Annual Meeting on all occasions except one in the association's history.

Changes in the pattern of the Annual Meeting are likely in the long run to be less important than the constitutional reforms which have been put forward by the Committee of Review. At present, one of the most serious handicaps to the smooth functioning of the association is the division of authority among several bodies, none of which is elected by the members. The ultimate authority, the General Committee, is an exceedingly amorphous body. The Council is in principle partially elected by the General Committee but in practice is a self-appointed body on which past presidents and officers loom large numerically. Day to day decisions have, however, been taken in recent decades by a much smaller committee consisting of the president and the statutorily authorized general officers of the association. Ostensibly, the day to day work of the association is done by

a full-time secretary, but except in special circumstances he may easily find himself hamstrung by the hierarchy of committees with which he must work.

The proposals now put forward by the Committee of Review would for practical purposes replace the Council and the General Committee by a Governing Body which is smaller than either and which is elected by the membership of the association. The concept of an open election is in itself a considerable innovation and one which should help to fortify the spirits of members, all too often neglected by the organization in recent years. The re-constituted council which the Committee of Review would like to see would, however, not be concerned with the day to day management and planning of the association's affairs—that would be the work of a smaller executive committee. The intention seems to be that the members of the Executive Committee and its chairman should be appointed for three years or for some other comparable period, so that there will be some measure of continuity in the association's management. Plainly, if these proposals are eventually accepted, the association's president will become almost exclusively a kind of intellectual mayfly who makes one important public speech a year on the association's behalf, but who has no substantial role in the long-term conduct of the association's affairs.

In its proposals for change, the Committee of Review has advocated closer relationships with other organizations and societies, and the Royal Institution, the Royal Society of Arts and the Royal Society are mentioned by name. There is plainly at the back of the association's mind the possibility of sharing administrative and even living costs with other bodies. Among some members of the association, a great deal of interest centres on the possibility of using the Annual Meeting as a means of allowing learned societies and professional institutions to hold meetings outside London. The statement on the new proposals issued this week draws attention to the opportunities for the association that will arise if the EEC is enlarged later on this year.

Although the association makes very little of the financial crisis which, early in 1970, precipitated its present bout of self-criticism, it is clear that money remains a preoccupation. A year ago, the association was persuaded by the threat of an impending deficit to reduce its overhead costs, which led it to the ineptly handled sacking of an administrative officer. The long-standing difficulty with which the association has to contend is that subscriptions from members contribute very little to the overhead cost of operating the association, that fees for the Annual Meeting

do not cover the cost of the Annual Meeting even though a great deal of this is usually met by local subscription and in spite of grants from the Department of Education and Science and the Department of Trade and Industry which amount to £25,000 a year. The recent economies at the association appear to have staunch the flow of its own investments and endowments, but it now appears that there is no assurance that government grants will be continued after 1972.

The Committee of Review says that the total cost of the programme now advocated will amount to £50,000 a year, a calculation which takes no account of the cost of regional activities which are at present supported largely with local resources. By all accounts, the Department of Education and Science is to be asked for a continuing grant towards the essential expenses of the association.

The problems with which the Committee of Review has not dealt, no doubt because they are in any case inaccessible to a body largely concerned with forms and procedures, concern the style in which the association functions. In recent years, it has become a staid body, avoiding controversy whenever it could. For an organization dependent for its success on making a mark in public, this has necessarily been a great mistake. But the association has also been dogged by a great deal of bad luck or bad judgment. Many promising public discussions have, for example, been ruined by a disastrous choice of speakers. Only time will tell whether the framework now provided will allow the association to flourish or whether it will, alternatively, continue on its downward course.

The Committee of Review included: Sir Alec Cairncross, KCMG, FBA (Chairman); Dr J. D. Carthy (Director, Field Studies Council); Dr H. M. Finlaison, FRS (Deputy Chairman, British Steel Corporation); Sir Vivian Fuchs (Director, British Antarctic Survey); Dr A. H. Hughes (Managing Director, Arthur Guinness Son & Co Ltd); Sir David Martin, CBE (Executive Secretary, Royal Society); Sir Eric Mensforth, CBE (Chairman, Firth Brown Tools Ltd); Mr P. W. B. Semmens (Agricultural Division, ICI Ltd, Billingham); Professor G. E. Fogg, FRS (Department of Botany, Westfield College); Lord Rennell of Rodd, KBE, CB.



## NEW WORLD

## Nixon May Sell Out to Kennedy on NIH

from our Washington Correspondent

IN the past few days, the Nixon Administration has come close to capitulation in its struggle with Senator Kennedy's health subcommittee to preserve the National Institutes of Health from dismemberment. Kennedy, against the almost unanimous advice of the scientific community, has been pushing a proposal to take the National Cancer Institute out of the NIH and establish it as a separate agency.

Last week it became apparent that the Administration has agreed to legislation that is tantamount to acceptance of the Kennedy plan. In return, the major concession made by the Kennedy side is that the proposal will be put before Congress in the Administration's name, not Kennedy's.

If the deal is accepted by the health subcommittee at its meeting this week, the Administration will, it seems, be conniving at an arrangement that may ultimately dissolve the National Institutes of Health, unbalance and fragment the biomedical research endeavour, and delay the date at which unconquered diseases, including cancer, are overcome. The advantage of the compromise, however, is that the Administration will succeed in barring Kennedy, seen in the White House as a potential contender in 1972, from taking credit for what politicians on both sides have presented as a major advance against cancer.

The existence of the compromise was revealed, apparently by accident, at a public hearing last week before the Senate health subcommittee, thus affording an unusual insight into the way Congressional committees conduct part of their business behind the scenes. Elliot L. Richardson, Secretary of the Department of Health, Education and Welfare, of which the NIH is a part, was appearing before the subcommittee to testify in favour of a counterproposal put forward by the Administration on May 11. The counterproposal, in the form of a bill introduced by the senior Republican member of the subcommittee, Senator Peter H. Dominick, embodies the plan announced by President Nixon last month (see *Nature*, May 14, 1971).

Nixon's plan would have instituted a "Cancer Cure Program" under which the National Cancer Institute would have had its own budget and director but remain within the NIH; in addition, the President could have re-delegated his authority for the programme back to the Secretary of

Health, Education and Welfare—a stipulation that would in effect have allowed matters to stay as they are.

Richardson arrived at last week's hearing with testimony to explain why this plan (referred to as S.1828, from the number assigned to Senator Dominick's bill) made better sense from the medical and administrative points of view than the bill proposed by Senator Kennedy (designated S.34). Senator Gaylord Nelson, a member of the subcommittee opposed to the Kennedy proposal, started to question Richardson on the Administration's position but it soon became apparent that the document Nelson held in his hand represented a different Administration position from that described by Richardson.

It turned out that Nelson was reading from a private compromise drawn up a few days previously between staff members of the health subcommittee and Administration representatives. The compromise, dated June 8, was in the form of a bill to be introduced by Senator Dominick and to replace the bill he had introduced on May 11 embodying the Administration's counterproposals. (Dominick, as it happened, had not even seen the new bill drawn up in his name.)

The compromise bill is subject to change until voted on by the health subcommittee at a meeting which is scheduled to take place this week and would not ordinarily have become public until then. But it seems that both the Kennedy side and the Administration are agreed on the main terms of the compromise, which are "to establish a Conquest of Cancer Agency as an independent agency".

The compromise bill adds the phrase "within the NIH", but these words seem to be intended in a purely geographic sense. The compromise is in fact an amalgam of the Kennedy and Administration bills, S.34 and S.1828 respectively, which takes the number of S.1828 (meaning that it is an Administration bill) and the text of S.34. The clause in the original version of S.1828, which allowed the President to redelegate his responsibility for the authority to the Secretary of HEW, has been struck out from the compromise version.

Administration sources claim that the President may delegate his authority anyway, whether the bill allows him to or not, but this interpretation is likely to be resisted by the Kennedy side.

Apart from the question of redelegation, the compromise which the Administration has agreed to is almost word for word identical with the Kennedy bill to set up an independent cancer agency. By revealing the terms of the compromise bill, Nelson put Richardson in the ironical position of having testified in favour of a position

## Dark Undercurrents

A SIGNIFICANT statement against the proposal to institute an independent cancer agency was made before the health subcommittee last week by John A. D. Cooper, president of the Association of American Medical Colleges. Cooper warned of the "dark undercurrents of opinion which appear to be sweeping the national debate on the conquest of cancer into potentially dangerous waters". Such undercurrents included the belief that the key to conquering cancer "lies in the managerial efficiency and capacity of the medical-industrial complex". Cooper's warning was doubtless a reference to the industrial interest—and hence political pressure—with which the new agency as envisaged by the Kennedy Bill would become entangled. Apart from the large sums of money to be spent on building new cancer centres, the Kennedy Bill—and the new compromise—explicitly enjoins the new agency to "encourage and coordinate cancer research by industrial concerns". The stark truth, Cooper reminded the subcommittee, is that science is complicated and "the key to its secrets is not neatly wrapped, awaiting discovery, in an appropriations bill or in the medical-industrial complex".

Cooper also expressed deep concern over "the precedent that would be set by making the director of the program a presidential appointee requiring the advice and consent of the senate. This would seem to imply that the direction of the major research programmes of the NIH is basically a policy rather than a scientific function and thus a matter for political determination".

which the Administration had already abandoned.

The disadvantages of the Kennedy plan to set up a separate cancer agency, to which the Administration has now assented, are clearly articulated in the testimony delivered by Richardson at the start of the hearing. The primary purpose of keeping the National Cancer Institute within the NIH, the Secretary told the Senate subcommittee, "is to keep cancer research in close and constant contact with the mainstream of biomedical research of which it is an integral part. Such contact is in fact essential. . . . It would be foolhardy indeed to suppose that this interdependence of the medical sciences will not continue in the future. To create the optimum conditions for a major attack on cancer, the relationships that have been so productive in the past must be maintained. Moreover, the indivisibility of knowledge and understanding in the life sciences is such that research on other diseases will also have much to gain from close contact with a greatly expanded cancer research effort". Richardson went on to explain that another important advantage of keeping the National Cancer Institute within the NIH would be "to avoid the disruptive effect on the medical research community of scattered responsibilities for Federal leadership and support. It will continue to be possible to monitor the overall pattern of research support and to avoid competition and duplication between research programs sponsored by various Institutes. . . . It is very important . . . that the enlarged cancer effort should not be at the expense of research on other diseases and that it should not have the effect of draining competent researchers and research sources from work on other disease problems".

All these arguments have been put forward in one form or another by the representatives of scientific organizations appearing before the Kennedy health subcommittee, and they would probably be agreed to by the sizable body of opinion in the scientific community that wishes to preserve the National Institutes of Health as a single organization capable of coordinating research over the whole field of biochemical science. Yet at the time Richardson delivered this testimony the Administration had already agreed in essence to the very proposal against which these arguments were cited.

Why has the Administration capitulated in so abject a fashion to the Kennedy proposals? Simple political expediency, which throughout the campaign has been one of the White House's chief guidelines, seems to have played an important part. The Administration may have reckoned that what-



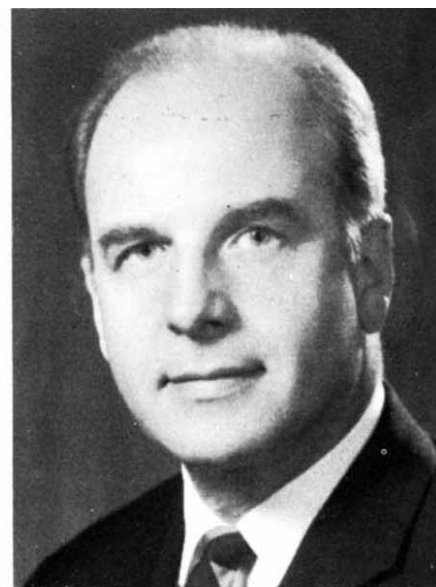
Elliot L. Richardson

ever bill is reported out by the Kennedy health subcommittee would probably pass Congress unless vigorously opposed, and that it was not worth risking a humiliating defeat just for the sake of keeping the NIH alive. The possibility of denying Kennedy credit for the bill by having it introduced in the Administration's name must have seemed an attractive alternative.

The compromise bill, if accepted by the health subcommittee at its meeting this week, will represent an outstanding victory for the sponsors of the drive to set up an independent cancer agency, as well as being a remarkable case study of how both Congress and the Executive can be manipulated by a determined pressure group. The case for an independent cancer institute, such as it is, was formulated by a body known as the National Panel of Consultants on the Conquest of Cancer. Appointed in April last year by a Senate resolution, the panel was chaired by Benno C. Schmidt, managing partner of a New York investment firm, and included as members 12 laymen and 12 scientists.

Last November the panel recommended in a report to the Senate health subcommittee that the National Cancer Institute should be set up as an independent agency endowed with an annual budget that would climb to \$1,000 million by 1976. (According to Senator Nelson at last week's hearing, the panel recommended this proposal by a 16-10 vote, since when three of the scientist members of the panel, Henry S. Kaplan, Joshua Lederberg, and Harold P. Rusch, have changed their minds, making a 13-13 split.)

Until the time of the panel report, the Administration had been resisting attempts in Congress to increase the already generous and probably suffi-



Senator Gaylord Nelson

cient federal expenditures on cancer research. During the appropriations process last year of the National Cancer Institute's budget, the Appropriations committee of the House of Representatives approved a budget of \$227 million, \$25 million more than the President's request.

Since the Administration was trying to live within its budget, Secretary Richardson wrote to the Senate Appropriations committee appealing for them to approve a budget for the National Cancer Institute some \$20 million smaller than that voted by the House. (Eventually the Institute wound up with a hefty \$230 million. The Office of Management and Budget might well have forbade the spending of the extra funds, as it had done when Congress had been similarly overgenerous the previous year, but for the publication in November of the cancer panel's report.)

The report at once gained a strong measure of support in both Houses of Congress—Kennedy was eventually able to announce that 52 senators were co-sponsoring his bill, and a counterpart measure in the House gained 132 sponsors—and the Administration's difficulty in perceiving that a breakthrough in cancer research was imminent and in need of extra funding was suddenly overcome. In his State of the Union message last January, President Nixon announced that an extra \$100 million would be made available for a programme to conquer cancer. When even this measure failed to buy off the support for the Kennedy plan, Nixon announced last month his unfortunately named "cancer cure program", under which the National Cancer Institute was to be elevated in name to the rank of a bureau. Nixon also announced at a White House press



conference his personal interest in the cancer cure programme, motivated, he explained, by the deaths from cancer of Senator William Taft, Foreign Secretary Allen Dulles and his Aunt Elisabeth.

The Administration's latest position may, at the worst, prove a sell-out of the National Institutes of Health, whose integrity, however, the White House has tried to guard subject to its own political interests. Assuming that the compromise Bill passes the Senate Health subcommittee and Congress, much will depend on whether the President is allowed to place the projected independent cancer agency under the care of the Secretary of HEW, in which case the harmful effects of its separation from the NIH will be somewhat mitigated, as well as on the nature of the man chosen to head the new institute.

Before the recent compromise, names such as those of Joshua Lederberg and Henry S. Kaplan—both of them scien-

tist members of the cancer panel who have since changed their minds on the panel's proposal—were being mentioned in Administration circles as possible contenders for the post. But the Administration may have had to yield to the Kennedy side even on the issue of having a scientist as head of the new agency. Even in the improbable event that the Senate health subcommittee rejects or radically alters the compromise bill, the Administration's readiness to sacrifice the proper management of biomedical research for a political expedient, at least in part, is a notable departure from principle. Kennedy's motives in pushing the bill are not so clear as his reasons for accepting the compromise; if he had listened with but half an ear to the scientific witnesses who appeared before his committee, he must be thankful to have his authorship removed from a bill that may in later years be credited with the destruction of the National Institutes of Health.

## Handler Speaks Out

by our Washington Correspondent

THE American Iron and Steel Institute in New York was the perhaps incongruous locale for a nevertheless steely speech delivered last month by Philip Handler, president of the National Academy of Sciences. Entitled "In Defense of Science", the speech castigated many of Handler's regular *bêtes noires* as well as some newer additions to the list including Administration manpower policy and some of the tactics used by cancer researchers in their efforts to increase government spending on the disease.

The Administration was criticized for its policies on scientific manpower—"should there not be appropriate jobs for [graduate students], our country will have fallen off the track of true progress"—as well as for its hypocrisy in washing its hands of the problem: Handler referred to the "disingenuous exclamations of governmental dismay when wholesale unemployment of technically trained individuals resulted from sharply decreased federal funding of applied research and development in the aerospace industry when, patently, the government itself was known to be the only customer".

The predilection for "relevance" that prevails in Washington Handler disposed of with the observation that if immediate social needs are to be made the arbiter of research endeavours, the scientific community would be doing "as generals do when they 'prepare for the last war'". The excesses of the current cancer lobby were also reproved. "Some scientists who should know better cannot resist the temptation to over-promise. Witness the behaviour of those who have recently indicated that only sufficient funding stands between us and definitive therapy of neoplastic diseases."

In a nod of recognition to those who criticize the traditional ethos of scientific detachment, Handler conceded he found "too facile" the attitude represented in a statement of Glenn Seaborg's that "Knowledge is born without moral properties . . . Man, not knowledge, is the cause of violence". Scientists, Handler said, "cannot escape the responsibility to make known the conceivable consequences of their newly gained understanding".

Recent speeches of the president of the National Academy have been tinged with a foreboding that even embraces quotations from such decadent authors as Petronius Arbiter; despite the embattled nature of his theme, Handler allowed the audience at the Iron and Steel Institute to entertain some hope of progress. Last year, he told them, "for the first time in recorded history, not a single case of smallpox was reported anywhere in the world. That event may go unnoticed in political history, but in the real history of mankind it represents one of man's truly great triumphs over his ever hostile environment".

## GRADUATE STUDENTS

### PhD Production Sags

by our Washington Correspondent

THE higher education production line which over the past decade has churned out PhDs in ever increasing numbers is now being put into reverse. The number of students enrolling in science and engineering graduate schools—which from 1960 to 1967 increased at an annual rate of 9 per cent—actually declined slightly between 1969 and 1970, according to statistics released this month by the National Science Foundation. The drop in enrolments has been particularly heavy at the leading graduate schools, which in proportional terms have suffered more than most from the scarcity of funds for scientific research and education.

The NSF survey also reports diminishing rates of growth both in the total faculty of science departments (which grew by 2.4 per cent in 1969–70 compared with 7.4 and 5.1 per cent in the two previous years) and in postdoctoral appointments. The latter have grown by 8.1, 10.3 and 0.6 per cent respectively in the past three years, the abrupt decline in 1969–70 presumably reflecting a saturation in the holding pattern whereby PhDs unable to find jobs elsewhere have been given temporary posts in their own department.

Based on responses from more than 3,000 science graduate schools in 227 universities, representing three-quarters of the total science enrolment in the United States, the NSF survey gives the following distribution of graduate students by area of science (figures in parentheses are the percentage change between 1969 and 1970): physical sciences 18 per cent (–3.2), life sciences 18 per cent (+1.7), social sciences 21 per cent (–0.3), psychology 8 per cent (+1.8), mathematical sciences 8 per cent (almost no increase) and engineering 27 per cent (–1.9). (Percentages refer to base of 189,000 enrolments.)

The decline in first-year enrolment is likely to affect not only the quantity but also the quality of future doctorates, since graduate schools of eminence have fared on the whole twice as badly as their less distinguished fellows. For instance, the ten leading physics graduate schools (as judged by the peer review system of the American Council of Education's Rating of Graduate Programs—see *Nature*, 229, 222; 1971) enrolled 34 per cent fewer students in 1970 than in the previous year, compared with an average drop of 12 per cent in other institutions. The average decline in enrolments over a range of fields was more than 6 per cent at the ten leading institutions in each field, compared with only 3 per cent in less eminent seats of learning.

## NEWS AND VIEWS

# Galaxy Clusters and X-Ray Sources

X-RAY astronomy continues to develop so rapidly that the wealth of available data is only beginning to be put into some sort of order by the theoreticians. Within the galaxy the range of sources covers types as diverse as the Crab Nebula, bright X-ray "novae" or flare stars, the recently detected X-ray pulsar in Cygnus and even the Sun. Perhaps this confusing flood of information is one of the factors which has encouraged some astronomers to turn their attention outside the galaxy, where experimental limitations provide a more stringent restriction on the number of phenomena which can be detected and thus make it easier to pick out patterns in the data.

Whatever the reason for their interest in extragalactic phenomena, the team of A. G. Cavaliere, H. Gursky and W. H. Tucker have indeed found some intriguing features in the data. These are described on page 437 of this issue of *Nature*, and pose as many questions as they answer, as is so often the case in this young branch of astronomy. Once again, the satellite Explorer 42 (UHURU) has been instrumental in providing the vital observations. In brief, the chief conclusion drawn from the observations of extragalactic X-ray sources is that there is a category of intense X-ray sources associated with clusters of galaxies, rather than with individual galaxies, or with quasars. This means that the X-ray producing region is not confined in a small volume of space—in the case of M 87 a region of the sky one degree across seems to be emitting around the prominent galaxy.

With the data so far available, it is not clear whether the regions of intense X-ray emission are at the central, dense parts of the galaxy clusters observed. Three sources of this new type of X-ray source do indeed seem to lie at the centres of galaxy clusters, and the very scarcity of data which makes it profitable for the theoretician to consider extragalactic phenomena ensures that, for the present at least, relatively simple theories explaining the phenomenon in terms of active dense central regions of galaxy clusters cannot be dismissed. The familiar idea that galaxies are born from an active region at the centre of a cluster is one that will certainly receive a stimulus from these observations.

But the other arguments are bound to be put forward by more conservative astronomers. The sources could arise simply from the superposition of X-radiation from many galaxies in the cluster, or this might come from one bright galaxy in each case. The latter possibility, however, seems rather dubious, particularly when it is seen that NGC 4847, the most likely candidate for such activity in the Coma cluster, would need to be emitting a degree of X-radiation totally inconsistent with optical and radio observations. Again, the Coma cluster contains several galaxies showing activity in the form of jets and other features, so that the superposition model is reinforced.

In this context, it is particularly interesting that the current issue of *Astrophysical Journal Letters* contains two reports on the detection of yet another flaring X-ray source within the galaxy (166, L69 and L73 ; 1971). Both

these reports, coming from groups working at the Massachusetts Institute of Technology, add weight to the growing conviction that there is enough intermittent strong X-ray activity in our galaxy to make it a respectable X-ray source in its own right when viewed from outside.

Undoubtedly this accumulation of information will swing opinion in line with the view that almost all galaxies are X-ray sources, and that dense clusters must therefore naturally be expected to appear as one diffuse source of X-radiation. But will the solution of the problem really be that easy? Cavaliere *et al.* point to other possible mechanisms, each of which fails to explain all the observed properties of these sources. If there is one thing which the explosion of high energy astronomy has emphasized, it is that there are no easy solutions to the problems confronting astronomers today.

## How Aspirin Functions

THE vast consumption of aspirin in modern medical practice is a powerful indicator of the therapeutic value of this drug. In spite of suspicions that there may be circumstances in which the use of aspirin has untoward consequences, it remains one of the safest and most valuable of drugs. It is therefore a great puzzle that so little has been known about the method of action of aspirin and related materials with similar therapeutic effects. A part of the reason, of course, is that the therapeutic value of aspirin lies in the generality of its effects. Not merely is it an analgesic but valuable in the treatment of inflammation of various kinds as well as the treatment of fever. With such a simple chemical structure, it is natural to look for some highly specific chemical interaction, but with such generalized therapeutic consequences, it is clear that this specific biochemical interaction must be widely distributed throughout the body. But where do these specific interactions take place?

Only in the past few years or so has it become apparent that the substances the biochemical function of which may be controlled by aspirin can indeed be isolated and studied. In 1969, Piper and Vane (*Nature*, 223, 29 ; 1969) demonstrated that inflammatory conditions in, for example, the lungs of guinea-pigs release materials which are themselves capable of stimulating the contraction of smooth muscles in isolated preparations. It was also clear that the same process was inhibited by aspirin and similar drugs. Inevitably, as it may seem, it has since turned out that the then unidentified substances are the ubiquitous prostaglandins. In short, there has been a growing suspicion that aspirin and related drugs may be therapeutically effective because of some relationship with the prostaglandins.

In next Wednesday's issue of *Nature New Biology* this tale is carried a big step further. In a group of three



articles, two groups from the same laboratory at the Royal College of Surgeons in London seem to have demonstrated conclusively that the specific action of aspirin consists of the inhibition of the synthesis of the prostaglandins  $\text{PGE}_2$  and  $\text{PGE}_{2a}$ . This has been confirmed both in experiments with lung homogenates (J. R. Vane, "Aspirin-like Drugs as Inhibitors of Prostaglandin Synthesis", *Nature New Biology*, June 23), with the spleens of experimental animals (S. H. Ferreira, S. Moncada, and J. R. Vane, "Indomethacin and Aspirin abolish Prostaglandin Release from the Spleen," *ibid.*) and even in studies of the production of prostaglandins in human platelets, where again it seems that the well-known effects of aspirin on the adhesiveness of platelets to glass, for example, may be explained by the inhibition of prostaglandin synthesis (J. B. Smith, and A. L. Willis, "Aspirin Selectively Inhibits Prostaglandin Production in Human Platelets," *ibid.*) The implication of these findings is plainly of great importance. One pleasing feature of the work is that the studies of the effects of aspirin on the production of prostaglandins in lungs and other organs were at first quite independent of those concerned with the effects of aspirin on circulating platelets, which were stimulated by the need to understand more fully the role of prostaglandins in the process of platelet aggregation as in the formation of thrombosis.

On the face of things, at least, it seems very much as if the demonstration that aspirin interferes with the local synthesis of prostaglandins will account for many of its therapeutic uses. In the first place, the way in which aspirin will reduce fever is linked with the observations in the past year or so that the prostaglandins are themselves among the most potent inducers of fever. (It remains, of course, to be seen what part is played by the prostaglandins in the regulation of body temperature in normal circumstances.) In exactly the same way, there is good reason to believe that the prostaglandins are concerned in the production of inflammation, so that a drug which inhibits the production of prostaglandins will be effective in these circumstances as well. But Vane considers that there is at present no reason to believe that the sensation of pain is mediated by the prostaglandins, so that there is no ready explanation for the analgesic activity of aspirin.

## PLATE TECTONICS

### Colliding Continents

from our Geomagnetism Correspondent

IMPLICIT in the theory of continental drift, and explicit in the detailed description of the phenomenon, is the break-up of continents. Several hundred million years ago the present continents were fragmented from one or perhaps two supercontinents and have been drifting across the Earth's surface ever since, though not necessarily continuously. Equally implicit in the continental drift theory, however, is the idea that some continents will eventually collide and even, if the drift forces are maintained in suitable directions, join. Understandably perhaps, the link-up of continents has received less attention than continental separation; but there is now convincing evidence of collision and adhesion. Within the present continents there are several linear belts of distinctive oceanic and geosynclinal deposits which apparently mark the boundaries (sutures) between once separated continents. The most conspicuous examples of sutures formed during the Wegenerian drift period are the Indus suture which defines the

boundary between the Indian segment of Gondwanaland and the Asian segment of Laurasia, and the ophiolites of the Alpine fold belt which mark the boundary between the Tertiary and Mesozoic blocks of Europe and Africa.

But if continental drift leads to the existence of sutures, the existence of sutures would seem to imply the occurrence of continental drift and, presumably, plate tectonic activity. In this sense therefore there is evidence for plate tectonic processes before the break-up of Gondwanaland and Laurasia because a Palaeozoic suture is known to exist in the Russian Uralides and what seems to be a Precambrian suture occurs in Ungava, Canada. To reinforce the evidence for Precambrian plate tectonics, Gibb and Walcott (*Earth Planet. Sci. Lett.*, **10**, 417; 1971) have now identified a second Precambrian suture in the Canadian Shield which suggests that the mechanisms of plate tectonic activity were active throughout at least the period 2390–1640 million years ago.

The newly discovered suture lies around the edge of the Superior Province which surrounds Hudson Bay to the east, west and south. This province is the largest unit of Archean

### Red Cells Inside and Out

HARD information on the structure of biological membranes is almost wholly confined to the nature of the lipid bilayer. The proteins, it has generally been supposed, form the sandwich with the bilayer as filling. Recently, however, it has become apparent that in the red cell, at any rate, little protein seems to be present on the outer surface. Labelling experiments with reagents that are unable to migrate through the barrier—most conclusively by one group of workers using an enzyme-catalysed iodination, which must certainly be confined to the outside of the cell—suggested, in fact, that only one protein component was available for reaction. This conclusion must now be re-evaluated in the light of a new study by Bretscher, which appears in the forthcoming issue of *Nature New Biology*.

Bretscher has found in the first place that the labelled component is not homogeneous: it consists of two proteins, which by chance migrate together in the standard detergent-gel electrophoresis system. Because one of them is a glycoprotein, it does not obey the law relating electrophoretic mobility with molecular weight, and can therefore be made to separate from its travelling companion by increasing the gel concentration. With a labelled reagent, which Bretscher has found does not penetrate the membrane, both com-

ponents are labelled from the outside. One is a protein of 100,000 molecular weight, the other of only 31,000, of which two-thirds is sialic acid. It is, in fact, the sialic acid that is modified by the reagent; when it is first split from the protein by a proteolytic enzyme, the residual molecule is not labelled by the reagent. When the cells are lysed, and the inside surfaces become available, the reagent goes to work, and modifies the whole range of proteins, including the two identified as accessible from the outside. Moreover when the sialic acid has been stripped away by pronase, so that the glycoprotein species fails to label from the outside, it still labels when the inside is also exposed. When labelling is from the outside, two radioactive peptides are generated after digestion of the proteins, which disappear if the prior pronase treatment with pronase is carried out. These peptides can be identified later in a fingerprint from the purified intact glycoprotein.

This seems then to leave no doubt that the glycoprotein projects like a skewer through the membrane. This is evidently also true of the other externally labelled, higher molecular weight protein, but this is the subject of another article. The glycoprotein is a major constituent of the membrane, each red cell having no less than half a million molecules of it.

rocks in the Canadian Shield and is itself surrounded to the north, east and west by the Churchill Province of mostly Proterozoic age. The suture thus forms the boundary between the Superior and Churchill Provinces, although the investigation of Gibb and Walcott was limited to that part of the suture which is exposed—a roughly east-west belt in Manitoba, a second east-west belt in the northern Ungava Peninsula and a northwest-southeast trending section in the Quebec-Labrador region (actually the Labrador Trough). In all, the suture is more than 3,200 km long.

The essential point about this belt is that it forms a distinctive set of rocks which are different from those of the surrounding Provinces and which are typical of plate accretion and consumption regions as defined by Cainozoic and Mesozoic plate tectonics. As only to be expected, the geology of such a region is complex and so it is not possible here even to summarize the features which distinguish this belt from its surroundings. In general, however, the relevant rocks are identified as a single unit because of the similarity of rock types, ages and position around the Superior Province. Their interpretation as a suture then depends on the juxtaposition of serpentinites and pillow basalts typical of plate accretion environments and engeosynclinal sediments typical of zones of plate consumption.

The interpretation of the Superior Province boundary in this way inevitably raises the interesting question of whether any part of the suture is oceanic crust or upper mantle material. For example, the Fox River sill, which lies in the Manitoban section of the belt, comprises ultramafic rocks whose lithology and association with pillow lavas is reminiscent of other areas of the world which have been so interpreted—the Troodos massif of Cyprus, the Camaguey complex of central Cuba and the Bowuta Mountains of Papua are the chief examples. Gibb and Walcott thus suggest that the Fox River sill is a slice of oceanic crust and upper mantle. But it is doubtful whether this or any other part of the suture is undisturbed oceanic crust not now underlain by silicic crust. The fact that continental collision almost certainly involves some marginal overthrusting makes it *a priori* unlikely that any undisturbed oceanic crust remains; and what experimental evidence there is tends to confirm this. Both geological and geophysical interpretations suggest that the suture zone rocks have been thrust upwards and are now underlain by continental crust. Seismic data recently obtained by Mereu and Hunter (*Bull. Seism. Soc. Amer.*, **59**, 147; 1969) in the Manitoban section, for example,

show that at the suture the crust thickens rapidly from 30–35 km under the Superior Province to 40–50 km under the Churchill Province; and gravity data in various parts of the belt suggest that continental crust, sometimes locally thickened, must lie beneath.

Finally, it is the view of Gibb and Walcott that the suture around the Superior Province is not likely to be the only one in the region but only the most conspicuous. Rock ages indicate that before the Hudson orogeny which deformed the sediments and volcanic rocks of the Churchill Province about 1700 million years ago, the Superior Province had been a craton for about 700 million years. The Churchill Province, on the other hand, seems not to have been a single continent in Aphebian times (2370–1640 million years) but a set of microcontinents separated by sedimentary basins, island arcs, trenches and seas. When these microcontinents came together they would presumably have formed a whole system of sutures; and indeed, current geological evidence suggests that this was the case.

## ORGANELLES

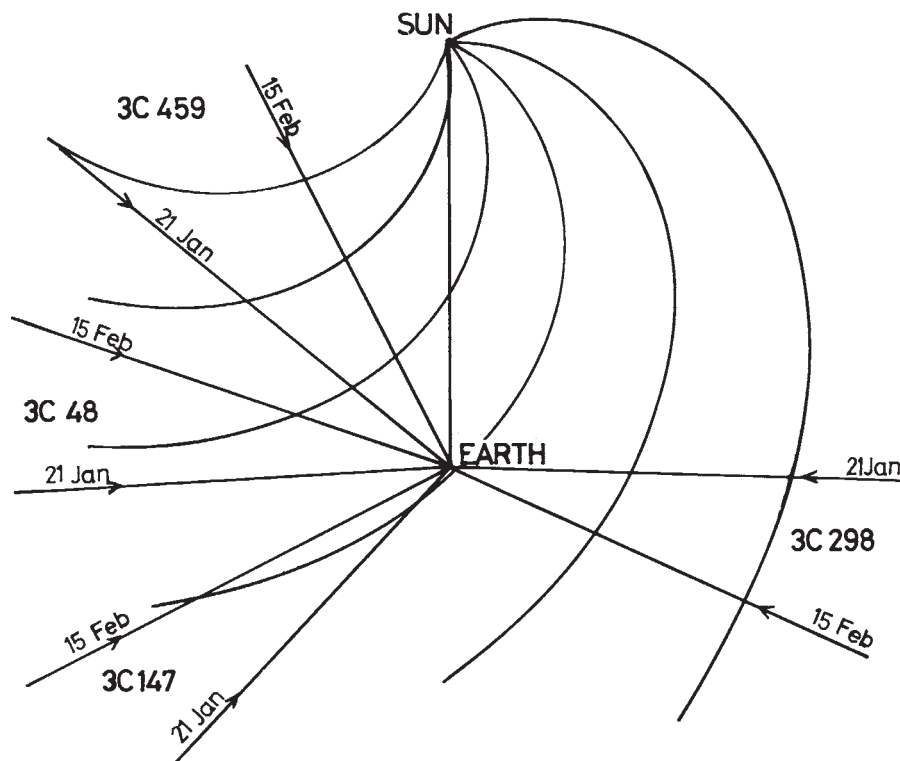
### Molecular Voltmeter

from our Membrane Correspondent

THE effects of ion-carriers such as valinomycin on the electrical properties of artificial lipid membranes have been the subject of intensive study in recent years. Apart from some preliminary measurements by Silman on that system so popular with membrane physiologists—the single-cell electroplax preparation—there do not seem to be any direct measurements of the effects of added ion-carriers on the electrical properties of natural membranes. This is not surprising considering the difficulties of trying to record the behaviour of the membrane current-voltage for an object as small as a single cell. Cell organelles are so tiny as to defeat the ingenuity of even the most skilled electrophysiologist, so that it is necessary to find indirect techniques for electrical measurements on organelle membranes.

This problem has recently been solved most elegantly for the thylakoid membrane by Junge and Schmid (*J.*

### Plasma Streams around the Sun



In the next issue of *Nature Physical Science*, Z. Houminer of the Cavendish Laboratory, Cambridge, presents compelling evidence for the existence of plasma streams corotating about the Sun. Such plasma streams were first suggested in 1968 but the statistics of previous experiments have not been sufficiently good to clinch the matter.

Houminer has shown that the inter-

planetary scintillation of radio sources as measured at the Earth in terms of the scintillation index is consistent with a rotating plasma stream as shown here in the illustration. The lines of sight of the four sources examined are shown at two dates during the observation period together with the position of a single corotating stream at two-day intervals.



*Membrane Biol.*, **4**, 179; 1971). Thylakoids are disk-shaped vesicles found within the chloroplasts of green plants. The thylakoid membrane contains a light-driven electric generator, together with pigments which, when there is a change in the electric field across the membrane, respond with a shift of their spectral absorption bands. This electrochromic shift can be used as a linear indicator for the potential difference across the membrane. Junge and Schmid induced such a potential difference using a short flash of light and measured the resultant voltage, in arbitrary units, by observing the electrochromic shift. They also similarly followed the decay of voltage with time. This decay was attributable to the membrane discharging through its own resistance and from its time course they were able to calculate the current. By carrying out this procedure in the presence of valinomycin and potassium ions they were able to construct a current-voltage curve for the effect of valinomycin on the membrane. It is gratifying to note that this curve is of the same form as that found for artificial lipid membrane.

In case it is thought that this approach is restricted to the thylakoid membrane, it should be pointed out that Witt (*Naturwissenschaften*, **10**, 514; 1969) and his co-workers have indicated that it ought to be possible to add the dye rhodamin-b to membranes and use its electrochromic shift as an index of electrical potential difference.

## NUCLEIC ACIDS

### Antianticodon

from our Molecular Biology Correspondent  
UNDER ordinary conditions a trinucleotide, such as ApApA, will not stick appreciably to the complementary trinucleotide, UpUpU. (Polymers are different: a catipede with a weak grip in each leg still hangs on hard.) On the other hand a tRNA will attach very strongly by its anticodon to a complementary trimer anchored on a ribosome, and even to a considerable extent to the free trimer. This inconvenient fact does not seem to have perturbed the voyeurs of the protein synthesis field one whit, but the more physically inclined workers in the area have been considerably exercised to account for it. The problem has now been illuminated by the work of Eisinger and his colleagues.

In a recent issue of *Nature New Biology* (**231**, 127; 1971), Eisinger, Feuer and Yamane introduced a superior new method of observing the binding of codon triplets to yeast phenylalanine tRNA. Where earlier workers had used the painful pro-

cedure of equilibrium dialysis, they apply a spectroscopic method, which has the merits of simplicity, of not interfering with the system in the process of measurement—a feature that removes a number of experimental uncertainties—of rapidity of execution and minute demands in material. It takes advantage of the presence of a unique, and strongly fluorescent base, Y, next to the anticodon. When an oligomer binds, the local change of environment is sufficient to engender an appreciable shift in fluorescence and this is made the basis of the binding measurements. By this means the thermodynamic parameters of the interaction of the RNA with its codon were determined, and it was not surprising to find a large unfavourable entropy term, arising from the conformational immobilization of the codon (as well, of course, as the association *per se*). Now it is generally supposed that the tRNA has a rigid tertiary structure, and it may be conjectured that the anticodon is designed

for binding in that it is held in the conformation of one strand of a Watson-Crick helix. In such a case this strand at least of the complex would contribute no unfavourable entropy to the binding process, because it would need to undergo no further conformational freezing, and, in this, the system would differ from one involving two conformationally mobile species, such as trinucleotides.

Eisinger (*Biochem. Biophys. Res. Commun.*, **43**, 854; 1971) has now hit on a way of verifying this hypothesis. If a pair of transfer RNAs could be found, the anticodons of which are complementary to each other, then they should associate without any loss of conformational freedom, and the binding should be very much stronger. Phenylalanine and glutamic acid tRNA are such a pair. The fluorescent technique again played its part; indeed, probably because the glutamic acid tRNA has a thiouracil residue next to its anticodon, with a long-wavelength absorption band, to which excitation

## Binding of Oestradiol in Uterine Nuclei

BIOCHEMISTS interested in the actions of hormones at the molecular level can be broadly classified into two groups; those who are intent on cataloguing the various effects of these agents on their respective target organs and those whose work is directed towards a search for specific hormone receptor sites in cells. To some extent the former group has always made it an act of faith that all the metabolic consequences of the action of a particular hormone stem from a primary site of action within the cell, whereas those who study hormone receptors tend to assume that these molecules represent such primary sites. Probably the best understood example of the interaction between a hormone and its target cell is the case of oestrogen binding to the mammalian uterus. Studies by Jensen and his colleagues have established that specific receptors for oestradiol exist in both the cytoplasm and the nuclei of the uterine cells. A report by G. Shymala Harris in next Wednesday's *Nature New Biology* now suggests that the structure of the DNA is important for the binding of oestradiol to the chromatin fraction of the nucleus in the mammalian uterus.

Harris shows that the oestradiol-receptor complex from the nuclei of mouse uterus can be solubilized by the action of an enzyme which digests away the DNA. The receptor complex thus released is similar to that obtained when the nuclear chromatin is disrupted by high ionic strength. This result may mean either that the oestrogen-receptor complex in the

nucleus is directly bound to the DNA or that the structural integrity of the DNA is essential for interaction of the complex with some other component of the chromatin. The implications of this finding are that the marked changes in uterine function resulting from uptake of oestradiol are initiated by direct interaction of the hormone-receptor complex with the genetic material.

The mere existence of "receptor" molecules which bind hormones does not prove, however, that the hormones exert their metabolic actions by such interactions. Indeed, it may be disadvantageous to the cell to possess a physiologically important site with a high affinity for a hormone because such tight binding could render a target organ relatively insensitive to variations in concentration of the hormone in the circulation. Furthermore, the concept that a hormone should act directly on an intracellular process may be a dangerous over-simplification of the subtleties of cellular regulation mechanisms. Biochemists who are familiar with the part played by cyclic AMP in the manifestation of the effects of a variety of hormones will appreciate that target tissues do not always possess physiologically relevant binding sites for the hormones within the cells. It is likely that a fuller understanding of the nature and significance of intracellular hormone receptors will come only from more extensive knowledge of the mechanisms of regulation in higher cells.

can transfer, the fluorescence of the Y base is quenched on binding. Expectations are gratifyingly and conclusively borne out: the association constant is between two and three orders of magnitude higher for the binding of glutamate tRNA than for the codon trinucleotide. Moreover, when this effect is broken down into its enthalpic and entropic components, the difference is seen to lie in the entropy, which is actually marginally positive for the association of the tRNAs. The complex indeed is so stable that it can be seen in gel electrophoresis. It is reasonable to conclude then that the anticodon loop of tRNA is indeed conformationally locked, so as to present one strand of double helix to its codon, and further that to generate sufficient free energy of binding the codon in the messenger is also held in the same state on the ribosome.

## GEODESY

### Low Level Talks

from a Correspondent

It is well known, from both scientific and popular literature, that in many parts of the world coastlines are emerging from or sinking into the sea, and that these processes have existed since the Earth first acquired its oceans. The causes, nature and some of the consequences of the relative movement of land and sea in south-eastern England were discussed at the Royal Society on May 26 and 27.

Although the first day was devoted to the "evidence for land subsidence" it was quickly made clear that some of the evidence was not unambiguous. Professor K. C. Dunham (Institute of Geological Sciences, London) traced the geological history of the London basin and Weald; from a sea level of +30 m, towards the end of the Pleistocene, the land rose to form the flood plain terrace of the Thames. On the basis of carbon-14 dating this trend was reversed during the past 4,000 years. One major uncertainty was concerned with the rate of the rise of the sea level during the most recent geological times. The work of Dr Jelgersma in Holland was frequently quoted in discussion; she favours a decreasing (but continuing) rate of rise, but not all the speakers agreed. Dr R. G. West (University of Cambridge) contended that during the past 10,000 years there was no evidence for subsidence, but that all of a 45 m rise in sea level could be attributed to eustasy, that is, a global redistribution of the water from melting ice caps. Gravity measurements on land and in the Dover Strait and adjacent waters, together with an analysis of geological

faults, were shown by Dr E. R. Shephard-Thorn (Institute of Geological Sciences, London) to provide continuity from England to the continent.

Secular trends in sea level derived from tide gauge records during this century were presented by Dr J. R. Rossiter (Institute of Coastal Oceanography and Tides, Birkenhead); they clearly indicate that relative to Scotland, southern England is sinking at the rate of 15 cm per century, and the Thames area by 25 cm per century. A comparison of the Second and Third Geodetic Levellings put the north/south tilt much higher at 50 cm per century between Newlyn and Dunbar, but Brigadier J. Kelsey (Ordnance Survey, Southampton) found no evidence for a Newlyn/Thames tilt.

One of the most direct consequences of the rising sea level has been to increase the risk of catastrophic flooding in London by storm-augmented tides. Furthermore, as Dr A. J. Bowen (Institute of Coastal Oceanography and Tides, Birkenhead) pointed out, the tidal range at London is increasing significantly by more than 30 cm per century, caused by the embanking of the river and other artificial changes. A fascinating account of the current pro-

posals for the Thames barrier was given by Mr R. W. Horner (Greater London Council), which reflected the coordinated efforts of specialist working parties in the fields. The many and varied repercussions of a barrier, the engineering background of which was given by Mr A. M. Beckett (Sir Bruce White, Wolfe Barry and Partners), were discussed in detail. Not all the studies are yet completed, but the various compromises involving location, engineering design and construction, and operation seem capable of avoiding insurmountable problems.

A meeting at the Royal Society which commenced with the geological history of an area, and ended with detailed designs for a civil engineering structure having enjoyed, *en route*, a highly critical assessment by a sociologist (Miss A. V. Akeroyd, University of York) of the archaeological evidence for subsidence, clearly had something for everybody. Its principal achievement was to demonstrate that in the United Kingdom the scientific expertise exists, both in government institutions and university departments, to tackle effectively environmental problems of considerable economic and social significance, given the right kind of coordination.

### Gravity Dissected

A NEW technique for exploring the Earth's gravitational field by analysis of satellite orbits has been successfully exploited by R. H. Gooding, who reports his work in Monday's *Nature Physical Science*. The Earth's gravitational potential is usually expressed as the sum of a series of harmonics defining the variations with latitude and longitude, and a detailed description of the field demands a large number of harmonic coefficients. The recent Smithsonian Standard Earth 1969 (*Smithsonian Astrophysical Observatory Special Report*, No. 315; 1970) has 296 coefficients, and the number increases as the square of the order of the highest-order coefficients, so that evaluating more and more coefficients would be very much a matter of brute force, possibly with unpleasant correlations to spoil the accuracy.

The need is for a fine probe which is responsive only to high-order harmonics: one such probe is the resonant satellite orbit, which follows the same set of ground tracks day after day. For example, a satellite in a polar orbit, which completes fourteen revolutions per sidereal day, that is, has an orbital period of 102.6 minutes, will follow a fixed set of fourteen ground tracks spaced at 25.7° in longitude. Such a satellite cuts the same swathes through the gravitational field day after day,

and the fourteenth-order components in the field will cause progressively increasing along-track perturbations in the satellite's motion. Stable resonant orbits of order 9, 12, 13 and 14 have already been most useful in studying the gravitational field.

Resonant orbits of order 15 have not hitherto been used, because they are so low (height 500 km or lower) that they are seriously affected by air drag, which quickly destroys an exact resonance. The new technique introduced by Gooding is to choose a satellite which passes slowly through the fifteenth-order resonance under the action of air drag, and then to analyse the resulting change in the inclination of the orbit to the equator, which depends on the value of fifteenth-order harmonics. Gooding determined the definitive orbit of the Anglo-US satellite Ariel 3 for the benefit of the experimenters, and he found an unexplained decrease in inclination of about 0.02° during the first three months of 1968. He has now analysed these results in detail, to obtain what are likely to be the best values yet for a set of lumped fifteenth-order harmonics. His work points the way towards similar analyses of satellites at other inclinations, allowing the determination of sets of harmonics of degree 15 and higher, uncontaminated by the effects of other harmonics.



## CELL COMMUNICATION

**Cells Swapping RNA**

from our Cell Biology Correspondent

THE notion that cells, when in contact, exchange nucleic acids and other macromolecules has never lacked enthusiastic advocates and has appeared in many guises, the most recent being Temin's provirus theory. But, to date, the only substantiated examples of intercellular chemical communication involve the passage of small molecules such as nucleotides—a phenomenon which Subak-Sharpe and his colleagues have aptly termed metabolic cooperation—and ions. There is, of course, ample circumstantial evidence to hint that the exchange of macromolecules also probably occurs but no conclusive and direct experimental evidence. The reason is obvious enough. In order to demonstrate the swapping of macromolecules between cells the experimenter has to be able to distinguish donor from recipient cells; he must be able to separate them and he must, above all, prove that the molecules being shunted around are indeed macromolecules rather than their low molecular weight precursors. These are difficult criteria to meet but not, it might be thought, insuperably difficult given ingenuity and patience.

Kolodny (*Exp. Cell. Res.*, **65**, 313; 1971) clearly shared this view; to achieve the separation of donor and recipient cells, he has exploited the fact that mouse 3T3 fibroblasts ingest tantalum, without apparent adverse effects, and as a result become considerably denser. In brief, he splits a culture of mouse 3T3 cells and allows one half to ingest tantalum and at the same time incorporate  $^3\text{H}$  or  $^{14}\text{C}$ -uridine of  $^3\text{H}$ -methyl-methionine. He then mixes and cocultivates these cells with the other half of the original population exposed neither to tantalum nor labelled NHA precursors. After varying periods of cocultivation the tantalum containing cells can be separated from the others by centrifugation through a Ficoll gradient. It then becomes a simple matter of assaying for radioactive RNA in the separated populations of cells.

In such experiments after cocultivation lasting 1 to 4 hours the recipient cells, those without tantalum, have 10 per cent of the TCA precipitable counts found in the donor, tantalum containing cells, and after 18–20 hours the recipients contain 23 per cent of the radioactivity of the donor cells. Granting that Kolodny's separation procedure is really as efficient as he claims, these results must mean that either labelled RNAs or labelled nucleotides are being transferred from cell to cell; cell fusion as a cause of the transfer can be ruled out.

Unfortunately, Kolodny's evidence

that it is indeed high molecular weight RNA that is transferred is indirect. For example, he shows that exposing the cells to actinomycin during cocultivation, at doses which inhibit RNA synthesis by 97 per cent, does not suppress transfer; he finds that the RNA precursor pools in both recipient and donor cells after cocultivation are not labelled above background; and he finds that thymidine incorporated into donor cell DNA does not find its way into recipients although  $^3\text{H}$ -methyl groups incorporated from  $^3\text{H}$ -methyl-methionine into donor RNA are transferred. Finally, Kolodny has shown that labelled ribosomal and transfer RNAs can be extracted from recipient cells after cocultivation.

Of course all these lines of evidence provide compelling but not conclusive support for the contention that intact RNA is transferred. To clinch the argument Kolodny must either show the transfer of a genetically marked RNA that could only come from the donor cells or else show that a physi-

cal barrier between donors and recipients, which is permeable to nucleotides but impermeable to RNA, blocks the transfer. The last has clearly not been heard of this fascinating story, and in his concluding remarks Kolodny hints of things to come by saying "preliminary experiments with SV40 transformed 3T3 cells using techniques described indicate a lack of RNA transfer between these cells".

## SPORTFISH

**Billfish Biology**

from our Marine Vertebrate Correspondent

IT is a paradox of marine biology that some of the least known fishes are the largest. Among the groups of which this is especially true are the billfishes of the family Istiophoridae, which include several well known sportfish such as the sailfish, the marlins, and spearfishes of tropical and subtropical oceans. Although these animals have

**Catenated R Factor DNA from Minicells**

THERE are numerous technical difficulties in the study of bacterial plasmids, not the least of which is the purification of their DNA. The DNA of antibiotic resistance factors (R) can be readily separated from the chromosomal DNA of *Proteus mirabilis* by buoyant density centrifugation but not from that of *Escherichia coli*, but as some R factors show different properties of stability and replication in these two hosts (Cohen *et al.*, *J. Mol. Biol.*, **50**, 671; 1970) it is of interest to be able to prepare the DNA from each.

The two standard techniques for separating R factor and *E. coli* DNA are caesium chloride-ethidium bromide centrifugation and bulk nitrocellulose adsorption. These methods both rely on the fact that R factor DNA exists as covalently closed circles and so they are unlikely to yield any other molecular forms of DNA. In next Wednesday's *Nature New Biology*, Cohen *et al.* describe a technique designed to avoid this bias. They utilize the observation reported last year by Roozen *et al.* (*Genetics*, **64**, 554; 1970) and Levy (*Nature*, **227**, 606; 1970) that  $\text{R}^+$  derivatives of a minicell-producing strain will segregate R factor DNA, but not chromosomal DNA, into their daughter minicells, giving a biological enrichment for R factor DNA.

Cohen *et al.* have isolated DNA from  $\text{R}^-$  minicells and have analysed it by centrifugation in caesium chloride with ethidium bromide. This has revealed three peaks of DNA; one with a density characteristic of covalently closed circular DNA, another with that of

open circular DNA and an unexpected third peak with an intermediate density suggestive of catenated R factor DNA. This classification is supported by the sedimentation pattern of the DNA on sucrose gradients, and by examination of the peaks with an electron microscope. The distribution of the R factor DNA between the three peaks varied from experiment to experiment, as did the proportion of the molecular forms within each peak, but in each case the densest peak contained predominantly supercoiled DNA, the intermediate peak contained singly or doubly open catenanes and the lightest peak contained open monomers.

Catenated DNA has been observed in mitochondrial DNA from several sources, and in *Salmonella* infected with P22, but in each case its origin is something of a mystery. Hudson *et al.* (*Cold Spring Harbor Symp. Quant. Biol.*, **33**, 435; 1968) suggest that they could arise from recombination or replication of circular DNA, or from an equilibrium between linear and circular forms. None of these explanations, however, is entirely satisfactory.

It is probably premature at this stage to speculate as to their origin from R factors for, as Cohen *et al.* point out, it is not yet clear whether or not they are just a peculiarity of minicell producing strains or of the minicells themselves. Should they prove to be of biological significance and not just the byproducts of recombination, then they may shed a little light on the somewhat obscure question of the form in which plasmids exist within the cell.

been fished for sport for half a century and commercially for half that time, knowledge of their biology is remarkably sparse and even their identification has been uncertain until very recent times.

Between 1964 and 1967 the East African Marine Fisheries Research Organization at Zanzibar conducted a survey of the tuna and billfishes in the equatorial western Indian Ocean, and as a result considerable advances in knowledge of the fisheries potential of the area were made. A study by N. R. Merrett (*J. Zool. Lond.*, **163**, 351; 1971) on aspects of the biology of billfishes from the area concentrates more on the biology of these fish than on fisheries aspects. One interesting result of this study shows that the five species caught in this area, the sailfish *Istiophorus platypterus*, the spearfishes *Tetrapterus audax* and *T. angustirostris*, and the marlins *Makaira indica* and *M. nigricans*, all seem to be conspecific with Pacific Ocean forms, a fundamental element if data from the better known Pacific populations are to be extrapolated to the Indian Ocean stocks. Only the *Tetrapterus* species show morphometric differences which can be interpreted as indicating population differences.

Merrett also examines growth rates so far as his material, and the difficulty of working with large fish at sea, would allow. Thus, for *Tetrapterus audax*, he found four year classes in his catches, and although it was not possible to establish the absolute age of the fish, during the four years they were available to the fishery they grew between 20 and 15 cm each year, with an approximate weight increment of between 27 and 21 lb. Length and weight frequencies were plotted for the other spearfish and the marlins and it was discovered that in the marlins the larger specimens are all females.

Estimates of the fecundity of the two *Tetrapterus* species and of *Istiophorus platypterus* showed that within each species there is considerable variation which seems to be linked with the size of the fish. Thus the ovaries of four specimens of sailfish showed a fecundity varying between 1.9 and 19.5 million ova, and two specimens of *T. angustirostris* had fecundities of 2.1 and 6.2 million. Clearly, many more observations will have to be made on the fecundity of billfishes before any final conclusions can be reached, but Merrett's figures seem to be the only firm data available and as such are of considerable value.

The migratory habits of these fish are well known and off the East African coast they seem to be related to monsoon periods. Thus Merrett found that *I. platypterus*, *T. audax*, and *M. indica* became more abundant during the

north-east monsoon, whereas *T. angustirostris* and *M. nigricans* appeared in greater numbers during the south-east monsoon. The two *Tetrapterus* species were most common offshore, and although like the other billfishes they are surface dwellers, they seem to prefer the open sea with depths of at least 250 fathoms. The marlins (*Makaira* spp.), however, were most abundant inshore over depths of up to 500 fathoms, and *M. nigricans*

seems to prefer still shallower water of up to 250 fathoms. This distribution according to monsoon conditions and bathymetric range is similar to that observed elsewhere for these billfishes. These and the other observations by Merrett add considerably to knowledge of these valuable commercial and sport-fish in the East African coastal area and confirm observations made in the Pacific by American and Japanese workers.

## Filaments or Ribbons in Mammalian Smooth Muscle?

THE controversy concerning the organization *in vivo* of the myosin in mammalian smooth muscle is brought to the forefront again by a pair of papers (Rice *et al.* and Somlyo *et al.*) appearing in *Nature New Biology* next Wednesday. Although electron microscopy and X-ray diffraction have clearly demonstrated the presence of ordered arrays of actin filaments in these muscles, the evidence concerning myosin filaments has long been ambiguous. It was only last year that Lowy and co-workers (*Nature*, **225**, 1053; 1970) first observed characteristic myosin reflexions in the X-ray patterns of both relaxed and contracting *Taenia coli* muscles. They also produced electron micrographs of the relaxed muscle showing ribbon-like structures, size 80 Å by 200–1100 Å in transverse section, which they suggested were the myosin-containing structures (*Nature*, **227**, 46; 1970). Many other workers, however, have observed thick filaments similar to those in striated muscle, and usually of diameter 150–200 Å. These have been observed in rigor and contracted muscle and in some non-physiological conditions, but only rarely in relaxed muscle.

Because different preparative methods have been used by the different groups of workers, the crucial point in evaluating the contrasting observations is to determine which of the methods does, in fact, preserve the structure of mammalian muscle *in vivo*. Rice and co-workers now report further electron microscope observations using their own techniques, and also examinations of the techniques used by Lowy and co-workers. Rice *et al.* fixed their muscles while they were bathed in an oxygenated Krebs-Ringer solution, in which procaine was sometimes added to ensure relaxation. Fixation was with 4 per cent formaldehyde; there was no indication of any tension increase. Several different mammalian muscles were examined in this relaxed condition and, contrary to their previous work, thick filaments were seen. Furthermore, in the rabbit portal-anterior mesenteric vein (MV) muscle, and also occasionally in *Taenia coli*

(TC) muscle, these filaments were observed in fairly regular arrays. There was an indication of square packing, and electron micrograph and optical diffraction measurements gave an interfilament separation of about 700 Å. Arrays of actin filaments were always observed. Similar features, but with many more thick filaments, were seen when muscles were fixed at 1.6 times their excised length. Garamvolgyi *et al.* (*J. Ultrastruct. Res.*, **34**, 135; 1971) also observed that thick filaments were considerably more numerous in stretched preparations.

The techniques used by Lowy *et al.* to observe the myosin X-ray pattern and the ribbon-like structures in the electron microscope have been criticized as being non-physiological. The muscles were allowed to equilibrate at 0° C in an oxygenated Krebs solution supporting a 10 g weight for 3–4 h before X-ray diffraction analysis or fixation for electron microscopy. This procedure produced a 3–10 per cent extension. Somlyo *et al.* have now examined both TC and MV muscles stretched to lengths up to 2.6 times the excised length, and/or in hypertonic solutions. Under these conditions they do observe ribbon-like structures, and these are more plentiful the greater the length and the more hypertonic the solution. They conclude that these conditions which abnormally reduce the interfilament spacing are responsible for the formation of the ribbon-like structures, and that the normal structure *in vivo* is represented by the arrays of thick filaments, which they observe. They also suggest that the width of the 144 Å meridional myosin reflexion in the X-ray diffraction pattern can be as readily accounted for by their observations of arrays of thick filaments, diameter ~180 Å, as by Lowy *et al.*'s observations of random distributions of ribbon-like structures. But because slight stretching increases the number of thick filaments visible, and more extensive stretching produces ribbons, it still seems a debatable question to what extent either of these structures is present *in vivo* in the relaxed unstretched muscle.



## POLLUTION

**Water and Industry**

from a Correspondent

In his introduction to the discussion on freshwater and estuarine effects of industry at the Royal Society on June 3 and 4, Sir Frederick Russell (Marine Biological Association, Plymouth) characterized the state of British rivers and estuaries as the combined result of overpopulation and misplaced priorities. Although the point was not directly taken up in the formal contributions, the effects of further population growth were clearly in the minds of several speakers.

Mr J. H. N. Garland (Water Pollution Research Laboratory, Stevenage) suggested that run-off from agricultural land added to the inorganic nitrogen content of the River Trent only during high flows; the steadier lower levels represent very largely the human contribution. On this basis, he calculated that its pollution load will be half as large again in the 1990s after the anticipated population growth of 1 per cent per annum; at an annual increase of 3 per cent, the Trent at Nottingham would be as filthy as its notorious tributary the Tame is now. This assumes no increase in the agricultural contribution although, in his paper on eutrophication, Dr J. W. G. Lund (Freshwater Biological Association, Ambleside) pointed out that British farmers could profitably use three times as much nitrogen as they do at present. It seems, nevertheless, that the river will be needed as a source of drinking water within 25 years. Mr T. E. Langford (CEGB Freshwater Biology Unit, Ratcliffe-on-Soar) showed that although Drakelow Power Station at Burton discharges cooling water 10° C hotter than the river, turbulence caused by pumping adds nearly 4 tonnes of dissolved oxygen per day. It was later agreed that 2–3 tonnes per day of the inorganic nitrogen are nitrified in the cooling towers of this station, which thus makes a positive contribution to the health of the Trent. Some polluting additions are less susceptible to amelioration or control—for example, the high concentrations of zinc, copper and nickel which appear in the Tame after heavy storms wash them from the rooftops of Birmingham.

Mr A. V. Holden (DAFS Freshwater Fisheries Laboratory, Pitlochry) listed sixty different pesticides which may get into freshwater in Britain, showing that although they never reach concentrations lethal to fish, levels at which the hatching of fish eggs is inhibited may be attained in otherwise clean rivers. In Loch Leven, a discharge of dieldrin (which, fortunately, has long since ceased) was accumulated in fish muscle

to the extent that this became unfit for human consumption. Egg laying by fish may also be prevented by copper and zinc at well below lethal levels, according to a survey by Mr R. Lloyd (MAFF Salmon and Freshwater Fisheries Laboratory, London) of problems in determining criteria for water quality. It seemed to be generally agreed by the meeting that such criteria, based on acute toxicity tests against a single species of fish, were not good enough. Mr Lloyd has found that ammonia causes an increase in the rate of urine flow in trout once it exceeded 12 per cent of the lethal concentration, and he has established that fishing conditions in various reaches of the Trent indicate a limit at about this level; it may thus form the basis of a non-lethal bioassay, but some speakers also stressed the need of criteria for invertebrates. It emerged in discussion that some rivers in the Clyde catchment remain fishless, although their waters are now adequately clean. This may be attributable to a poor invertebrate fauna, perhaps because toxic materials are still held in bottom deposits.

Professor J. E. G. Raymont (University of Southampton) opened the proceedings of the second day with a review of the condition of Southampton Water, which showed that it is not suffering too badly, although biological as well as purely planning considerations ought to be taken into account before any further urban development is permitted. An interesting feature is

the large American clam *Mercenaria mercenaria*, the status of which has been elevated from that of a rare immigrant in 1957 to a dominant bivalve which, especially in areas warmed by effluent from Marchwood power station, supports a commercial fishery. Possible problems arise from the ability of these and other filter-feeders to accumulate toxic pollutants even from very low concentrations in the water or sediments.

Dr A. Nelson-Smith (University College, Swansea) dealt with the sources, effects and treatment of oil pollution in estuaries. He concerned himself chiefly with investigations in Milford Haven, but also referred to a saltmarsh in Southampton Water where similar low concentrations of oil in large volumes of refinery effluent have accumulated to the point of denuding 90 acres of both vegetation and several inches of loose sediment. Shores which are reasonably rich in marine life can recover from a single oiling but, within oil ports, pollution is more likely to be of this damaging chronic or repetitive kind. Another rather specialized form of pollution was discussed by Dr T. H. Pearson (Scottish Marine Biological Association, Oban) who has studied the effects of wastes from a paper mill at the head of a sea loch. Because the sea loch already has local deposits of natural cellulose waste in the form of leaf litter, the fauna is preadapted to deal with pulp wastes, and has merely spread more widely.

**Laser Raman Spectroscopy**

DURING the past decade light scattering research has been revolutionized by the introduction of the laser. The most widely investigated and useful form of light scattering is Raman scattering, which involves the inelastic scattering of light in media. So far most of the work has focused on the formation of vibrational modes of excitation, but the technique is not confined to this and other forms of excitation are now being studied, for example, an investigation of the pure rotational spectra of gases can provide information on the dimensions of simple molecules. Scattering from magnons or spin waves has furthered understanding of antiferromagnetic materials and their phase transitions. Light beams may also be scattered from plasmas and studies have been made on both gaseous and semiconductor plasmas.

With the high power now available from lasers interpretable Raman spectra can be obtained from dilute systems of molecules or molecular ions in liquid or solid solution. An excellent example of a matrix isolation study using Raman spectroscopy is reported

by Ozin and co-workers in next Monday's *Nature Physical Science*. They have obtained Raman spectra from  $\text{SeO}_2$  molecules isolated in a solid carbon dioxide matrix at 4.2 K. By measuring spectra at various higher temperatures they were able to observe the results of diffusion controlled chemical reactions including the formation of the dimer  $(\text{SeO}_2)_2$  and higher polymers.

The matrix isolation technique using molecular crystals was originally developed to deal with problems of molecular structure using infrared spectroscopy. Notable success has been achieved in the area of free radical spectroscopy and the sole evidence for the existence of numerous fragments testifies to the effectiveness of the method. The combination of infrared and laser Raman spectroscopy considerably aids the assignment of the symmetry of molecular species. It is clear that a profitable field of study will be opened up as more workers master the problem of good sample preparation which is so essential for successful Raman spectroscopy.

# Modelling Cities as Dynamic Systems

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**Most attempts at building mathematical models of cities treat such systems as if they are in static equilibrium. But models which simulate the dynamics of change in cities seem to be more relevant to urban research and planning. The design and application of such a model are described in this article.**

For ten years, urban researchers have been attempting to describe the structure of cities by means of mathematical models. Although interest has undoubtedly been stimulated by advances in computer technology, such developments are part of a wider transformation in the methodology of the social sciences. In sociology, geography, economics and government, efforts have been made during the past decade to develop more systematic approaches using analogies from the natural sciences and the language of general systems theory<sup>1</sup>. Planners have also been excited by the prospects of using these systematic methods to forecast the physical, economic and social futures of cities, regions and nations.

Three principal roles for mathematical models of cities can be distinguished. First, such models have been developed to help in refining and experimenting with hypotheses about the structure of cities; they form an essential part of theory development in urban research. Second, models have been used to provide methods for educating planners in urban theory. Third, and perhaps most important, the models can be used in practical planning studies to help predict the likely consequences of planning or not planning the future of cities.

## Developments in Modelling

The first attempts to model the urban system were made by traffic engineers. Their models, based on various theories about traffic flow, were highly successful and led to more ambitious attempts to model other subsystems of the urban system such as the housing market and the location of retailing activity. The theories of location and spatial competition, firmly established in urban geography and economics, were the basis of these partial models, although at that time urban researchers were beginning to stress the interdependent nature of the subsystems which comprise the city. Consequently, model builders began to build more general models, attempting to integrate the housing, retailing, and industrial sectors with the transport system<sup>2</sup>.

These models were first developed in the early 1960s in North America and followed previous developments in transport systems analysis. The chief focus of this research was on the spatial variation of the pattern of activities such as popu-

lation and employment and on the interactions between such activities. The technique of modelling interaction using the so-called gravity model, derived by analogy with the Newtonian concept of gravity and, more recently, with the concept of entropy in statistical mechanics<sup>3</sup>, was central to much of this research and reflected the concern of the model builders with the interdependencies within the urban system.

## Static or Dynamic Models?

In spite of the enthusiasm of social scientists for these systematic approaches to urban research, progress has been extremely slow. The immensity of this kind of research effort was not anticipated by the model builders, who often did not appreciate the difficulties of collecting the data required to operate the models and the limitations imposed by computer capacity. In building such models, cities are usually divided into homogeneous areas or zones, and the smaller the size of zones, the greater is the descriptive power of the model. But as the number of zones increases, more and more detailed data are needed and computer storage requirements increase, often exponentially.

An even more important problem is conceptual. Nearly all models designed so far describe the city as a static system. Such models simulate the structure of the city at one point in time but ignore the processes which have generated the structure. Clearly any such model is a gross simplification of the real world and is likely to be of only limited use in a practical context. In building static models, model builders have also encountered severe problems concerned with the measurement and observation of certain variables. It is extremely difficult, for example, to find suitable variables which measure locational attraction in a static sense, for continual changes in such variables with time account for the present structure of the city<sup>4</sup>. Furthermore the performance of these static models has been disappointing in comparison with the more successful traffic models. Because these models lack historical perspective, they are difficult to use in forecasting<sup>5</sup> and planners have become somewhat disillusioned with their development.

If the early promise of mathematical modelling in urban research and planning is to be realized, it is not only desirable but essential that model builders should attempt to simulate the many complex processes which affect the structure of the city. To be sure, it is easy to see why model builders and theorists have ignored dynamics, for besides the increases in data and computer storage resulting from an additional dimension in such models, it is difficult to collect the necessary time series data required in testing and validating the models. These difficulties in observing processes of change have also led to problems in formulating meaningful hypotheses about the dynamics of cities and setting up relevant experiments.

Elsewhere in the social sciences, the dynamics of processes have not been ignored. A large part of economic theory, for example, is concerned with the modelling of economic



processes such as trade cycles and with tracing the effects of various fiscal policies on the national economy<sup>6</sup>. Furthermore, sociologists have begun to simulate changes in attitudes in small groups with models based on systems of differential equations<sup>7</sup>. Although such analysis can be used as a starting point from which to direct research into the dynamics of city systems, it would be misleading to imply that no dynamic models of cities have yet been built; there are two which are worthy of mention. The first—the Time Oriented Metropolitan Model—is a static spatial model which is designed to simulate changes in the structure of activities in time intervals of 5 yr or more<sup>8</sup>. The second model, designed by Forrester, is based on his concepts of industrial dynamics and simulates the processes of change in a hypothetical city in 5 yr intervals over a 250 yr period; the model is, however, not spatial and does not recognize that the structure of activities in a city can be explained in terms of spatial interaction<sup>9</sup>. Although these examples show that the dynamic processes in cities can be simulated, at least in part, the models are not comprehensive in their treatment of both time and space as essential determinants of the structure of cities. What is required is a more general approach which integrates the concept of spatial interaction with the processes of change.

## Design for a Dynamic Spatial Model

The model which is being built at the University of Reading is designed to simulate the changing structure of activities and interactions between activities at intervals of one year over a 15 yr period. The model makes a distinction between activities such as population and employment, and land uses such as housing and industry in which these activities are located. The employment sector is further subdivided into basic employment and service employment. The basic category comprises employment in resource-based and manufacturing industries whose location does not depend on other activities in the city, whereas the service category includes employment which "serves" basic employment or population and is located in relation to these two activities. Basic employment is an input to the model and the theory assumes that population and service employment can be generated and located in zones of the city from this given distribution of basic employment. The theory, which is well known in regional and national macroeconomics, is known as the economic base hypothesis.

The importance of this hypothesis in designing a dynamic spatial model involves the process used to generate population and service employment from basic employment. The repercussions which result from this process are manifest both spatially and temporally and the model is designed to simulate the complex nature of these repercussions and their effect on the structure of activities in the city. If, for example, a new steel mill (part of the basic sector of employment) is located in the city, the services and population which support it do not locate immediately. It takes time before the demand for the services and associated population is satisfied. Such repercussions die away with time and one possible way of modelling this process is by the simple equation

$$E_t = B e^{-\mu t} \quad (1)$$

where  $E_t$  is the amount of activity generated at time  $t$  after the initial input of activity  $B$ . In this example,  $B$  could be basic employment associated with the steel mill and  $E_t$  the services generated at time  $t$  which are the direct or indirect repercussions of locating this steel mill. The total amount of activity  $E$  associated with  $B$  can be found by integrating equation (1) over  $t$

$$E = B \int_0^{\infty} e^{-\mu t} dt \quad (2)$$

In fact it is more convenient to use a discrete analogue of equation (2) based on a converging geometric series. Total activity  $E$  is generated from  $B$  as follows

$$\lim_{n \rightarrow \infty} E = B(1 + \lambda + \lambda^2 + \lambda^3 + \dots + \lambda^n); \quad 0 < \lambda < 1 \quad (3)$$

In the present model design each term of the series presented above corresponds to one time interval although equation (3) is only an abstracted summary of the model's dynamic process, for in each time interval a large part of the simulation is concerned with the allocation of activities in space. The services and population generated by the steel mill do not necessarily locate in the same place as the steel mill; the services are more likely to locate in existing service centres, and this in turn affects the location of population and further services.

In simulating the repercussions of activity, a distinction is made between the stocks of activity observed at any one point in time and the changes in activity between these points. As well as modelling the absolute changes in activity, changes in the location of the existing stock of activity are also simulated. In fact in most cities at least half of all change can be accounted for by the relocation of existing activity, and this model is designed to simulate such internal migrations. The relocation of existing activity is handled using the same mechanisms designed to locate new activities in the region. For example, in terms of equation (3), the variable  $B$  could be composed of new activity and existing activity, although a fairly elaborate accounting procedure is then necessary to avoid any double counting of activities.

A diagram of the activities and land uses which are linked together by the model is presented in Fig. 1. The model is divided in five submodels dealing with the spatial location of activities. Population and service employment are located using gravity models in which the amount of activity located in an area varies directly with the locational attraction of the area and inversely with the cost of travelling to the area. In the population sector, locational attraction is a function of existing floorspace and available land in a zone and two further submodels are used to predict these levels of attraction. Finally, a submodel is used to predict the location of that part of the basic employment sector which can be explained in terms of the location of population and services.

The model is formulated mathematically as a system of difference equations which relate population, service employment and basic employment together through time by the economic base hypothesis, and through space by the gravity models which simulate the flows between the various activities. Although the submodels used to locate the activities are gravity models, that sector of basic employment endogenous to the model is located using a linear model

$$\Delta Y_i^{t+1} = \sum_j \alpha_j X_{ij}^t + \sum_k \theta_k \Delta Z'_{ik} \quad (4)$$

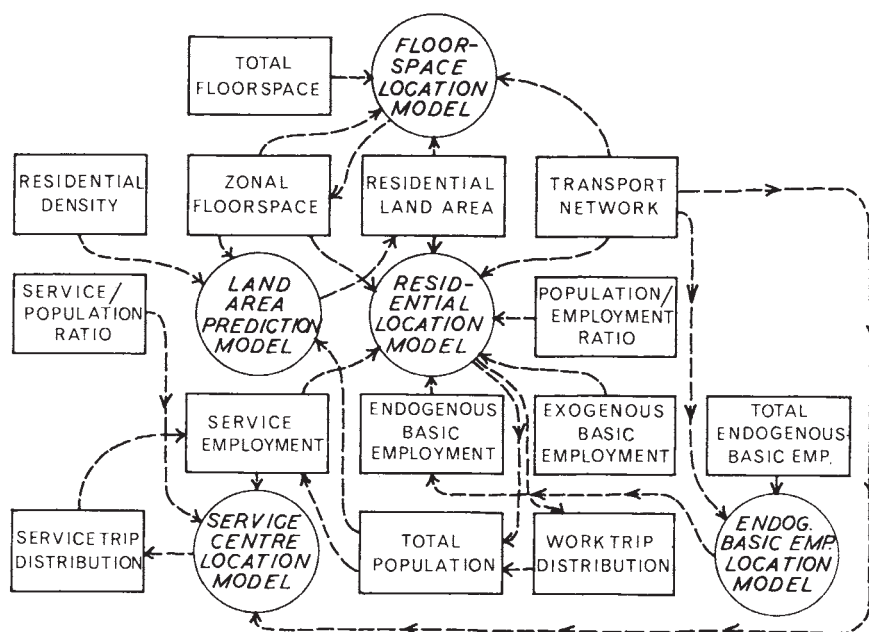
where  $\Delta Y_i^{t+1}$  is the change in endogenous basic employment between time  $t$  and  $t+1$ ,  $X_{ij}^t$  are independent variables ( $j$  measured at time  $t$  in zone  $i$ ) and  $\Delta Z'_{ik}$  are changes in independent variable  $k$  between times  $t-1$  and  $t$  in zone  $i$ ;  $\alpha_j$  and  $\theta_k$  are parameters of the equation. The specific form of equation (4) being applied at present uses as independent variables stock of population, total employment observed at time  $t$ , and changes in total basic employment between time  $t-1$  and  $t$ . It is eventually hoped to test different forms of this equation.

The type of gravity model used to simulate interactions between various activities can be best illustrated in the context of the interaction between the population and employment sectors. The change in number of work trips  $\Delta T_{ij}^{t+1}$  between zones  $i$  and  $j$  and times  $t$  and  $t+1$  is predicted from

$$\Delta T_{ij}^{t+1} = A_i^{t+1} \Delta E_i^{t+1} \delta_j' (\sigma L_j^t + (1 - \sigma) F_j^t) e^{-\beta c_{ij}^t} \quad (5)$$

$$A_i^{t+1} = [\sum_j \delta_j' (\sigma L_j^t + (1 - \sigma) F_j^t) e^{-\beta c_{ij}^t}]^{-1}$$

Fig. 1 Organization of the components in the simulation model.



where  $\Delta E_i^{t+1}$  is the change of employment in zone  $i$  between  $t$  and  $t+1$ , and  $c_{ij}^t$  is a generalized cost of travel between zones  $i$  and  $j$  at time  $t$ .  $L_j^t$  and  $F_j^t$  are the amounts of land and floorspace available for residential development in zone  $j$  at time  $t$ .  $\beta$  and  $\sigma$  are parameters of the submodel. Both land and floorspace are used as proxies for residential attraction and these variables are in turn estimated by submodels before they are fed into equation (5). In the model there are constraints on the amount of population which can be accommodated in any zone  $j$ ; the parameter  $\delta_j^t$  acts as a brake to ensure that such constraints are not violated, for if such constraints are infringed in zone  $j$  at time  $t$ ,  $\delta_j^t$  is set equal to 0; otherwise the value of this parameter is 1. The change in population residing in  $j$  between  $t$  and  $t+1$  can be found by summing equation (5) over  $i$  and scaling the result by a constant  $\gamma$ . Thus

$$\Delta P_j^{t+1} = \gamma \sum_i \Delta T_{ij}^{t+1} \quad (6)$$

Equations with a form similar to (5) and (6) are used to locate service employment in service centres. Different forms of these gravity model equations imply different hypotheses about the workings of the city system<sup>10</sup> and, as part of the research design for the model, different forms of equation (5) will be tested and the sensitivity of different parameters evaluated.

A brief summary of the model's simulation process suffices to show how these different submodels are linked together. In each time interval, the equations are solved sequentially starting with the location of endogenous basic employment given by equation (4). The levels of locational attraction are then predicted and this is followed by the location and generation of service employment and population using the gravity model equations (similar to equations (5) and (6)). This sequence is terminated by an accounting procedure in which the net differences within the time interval are computed and, finally, the model's predictions are tested to see whether or not the constraints have been violated. The simulation procedure is then repeated for the next interval of time. In the existing design of the model, it appears that the repercussions of the location of basic employment die away to insignificant levels after ten intervals of time, and any further repercussions are small enough to be ignored. In terms of equation (3) an approximate value for  $E$  is obtained when  $n$  is 10; therefore in any interval of time, change is composed of

a spectrum of activity initially generated in all the previous ten time intervals. The model provides an interesting contrast with static models which simulate the city as if it is in equilibrium. The assumptions behind this dynamic model show that the city is always in disequilibrium for at any instant in time there are still repercussions in the model which have not yet worked themselves out. This appears to be a more tenable hypothesis, for the equilibrium state implied by the static models is somewhat unrealistic.

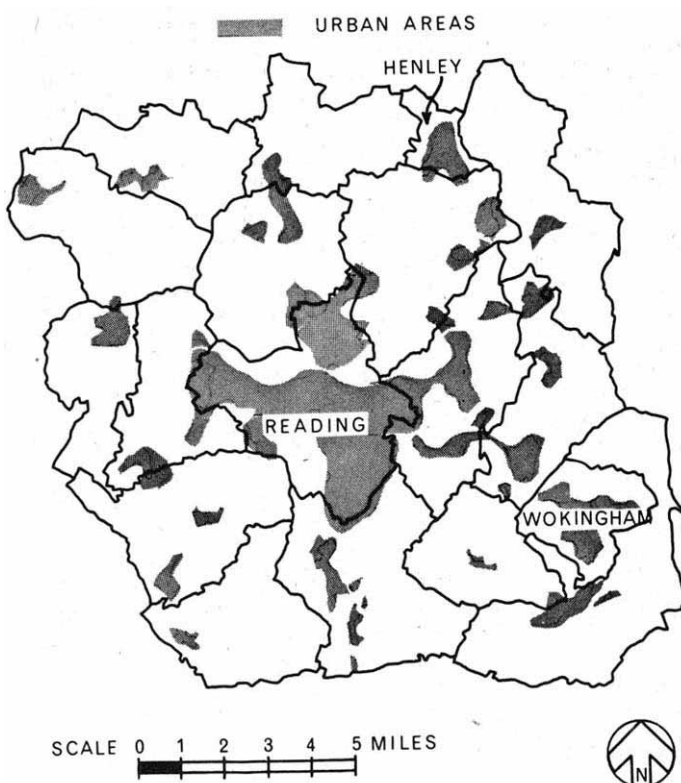


Fig. 2 Zoning of the Reading urban region.



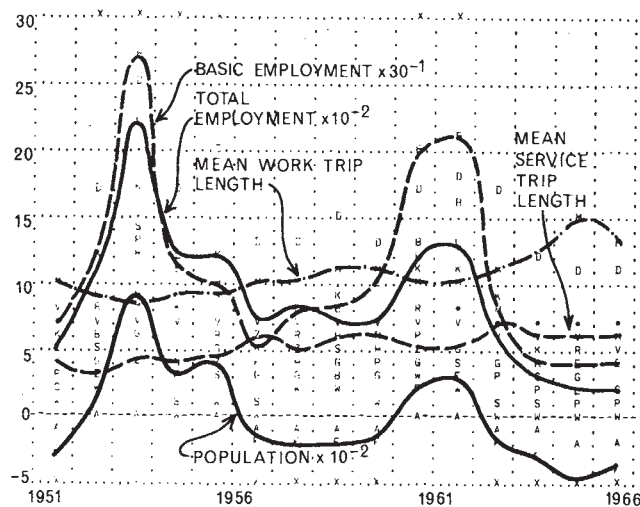


Fig. 3 A typical profile of changes in activity between 1951 and 1966 predicted by the model for the zone of Reading.

## Applications of the Model

As in any science, validation and refinement of the hypothesis implied by the model can only be accomplished by testing in a real situation. The model has been built using data from the town of Reading and its immediate economic hinterland. This small urban region is shown in Fig. 2; the system has been partitioned into 18 zones for modelling purposes. The model is designed to simulate the changing structure of activities in these 18 zones at intervals of one year between 1951 and 1966. The choice of this time period and the zone geometry is related to the availability of data; in this application, the chief data source is the population census, although this data base has been supplemented by information collected by local authorities. Even at this coarse level of description, there are deficiencies in the quality of the data, and the computer storage required by the model is considerable.

The process of experimentation connected with the design of this type of model is usually called calibration. The chief purpose of calibrating the model is to estimate the values of parameters which control the model's locational simulation, and the repercussions of activity through time. An important part of the calibration process, however, is to assess the sensitivity of the model to changes in the parameter values, and from such analysis to evaluate the design of the model's individual parts. The model produces a considerable amount of output in terms of the level of stocks and changes in activities and flows at every time interval in the simulation period. These data are plotted for each zone and Fig. 3 presents a typical plot of changes in activities between 1951 and 1966 for one zone. This type of graph is being used to assess the effects on other activities in space and time of changing the level and location of one particular activity.

At present the model is being calibrated using two different techniques of statistical estimation. First, the parameters of the linear model given by equation (4) are estimated using multiple linear regression analysis. As this analysis is applied outside the main framework of the model, different types of regression are being developed which take account of the influence of time in the analysis in different ways<sup>11</sup>. Second, the parameters of the gravity models are being estimated using a gradient search procedure. Such a procedure is necessary because these equations are intrinsically non-linear, and analytic methods of parameter estimation cannot be used. For example, in equation (5) it is necessary to find the values of the parameters  $\beta$  and  $\sigma$  which optimize the model's fit to real world data. First approximations to the values of  $\beta$  and  $\sigma$  are fixed either arbitrarily or from past experience, and the goodness of fit of the model is evaluated

in the neighbourhood of these first approximations. The gradient search procedure is concerned with finding the best directions in which to change the two parameter values in the search for an optimal fit. There are difficulties in applying this procedure, for it is possible that the search will end at a local rather than global optimum. When these procedures are used, part of the research effort is concerned with finding meaningful statistics which measure the model's goodness of fit to reality. At present, statistics based on the correlation coefficient and the chi-square distribution are being used to measure this fit. This area of calibration has been somewhat neglected by model builders and there is an urgent need for further research into appropriate statistical techniques for land use models.

Although the model is at present being developed as a vehicle for generation and testing of hypothesis about the dynamics of cities, it is hoped that it will be used in forecasting. Such dynamic models will probably be useful in predicting the short term consequences of planning decisions, and for the first time it may also be possible to answer such questions as: "What would have happened if the city had expanded in one particular direction or another?" In the Reading region there have been some important planning decisions in recent years which are likely to alter the structure of activities in this area quite radically in the future. The M4 national motorway, for example, is being built across this area and already this is generating additional demands for housing and industrial land along the proposed route. The model can be used to forecast the effect which such an addition to the transport system will have on the location of existing and future activities. By changing the generalized costs of travel along different routes specified in equation (5), this will alter the distribution of trips, and ultimately the changes in population given by equation (6). It will also be possible to test the recent proposals made by the South-East Joint Planning Team who suggested that large scale expansion of employment and population was desirable in the Reading area. By locating new basic industries, the repercussions on the spatial distribution of other activities can easily be traced with the model, and any undesirable effects can be isolated. A more important but longer term goal in the development of this kind of model is its application in the town and regional planning process, for it seems possible that such a model can be used to help planners in the design of optimal settlement patterns.

Although the model is a highly simplified abstraction of reality, it appears that greater insights into the structure of cities can be achieved using a dynamic rather than a static approach to modelling. Apart from the detailed technical problems of fitting the model to real world data, which have yet to be resolved, the model is already providing a useful method for the analysis of urban problems concerned with housing and transportation. If this methodology is further developed in planning practice, then the potential of a more systematic approach to the study of the city may be realized in terms of better planning.

- <sup>1</sup> McLoughlin, J. B., and Webster, J. N., *Environ. and Planning*, **2**, 369 (1970).
- <sup>2</sup> Lowry, I. S., *Model of Metropolis*, RM-4035-RC (Rand Corporation, Santa Monica, 1964).
- <sup>3</sup> Wilson, A. G., *Nature*, **220**, 963 (1968).
- <sup>4</sup> Broadbent, T. A., *Environ. and Planning*, **2**, 469 (1970).
- <sup>5</sup> Batty, M., *Regional Studies*, **4**, 307 (1970).
- <sup>6</sup> Baumol, W. J., *Economic Dynamics* (Macmillan, New York, 1951).
- <sup>7</sup> Coleman, J. S., *Introduction to Mathematical Sociology* (Free Press, New York, 1964).
- <sup>8</sup> Crecine, J. P., *A Dynamic Model of Urban Structure*, P-3803 (Rand Corporation, Santa Monica, 1968).
- <sup>9</sup> Forrester, J., *Urban Dynamics* (MIT Press, Cambridge, Massachusetts, 1969).
- <sup>10</sup> Wilson, A. G., *Entropy in Urban and Regional Modelling* (Pion Press, London, 1970).
- <sup>11</sup> Rogers, A., *Matrix Analysis of Interregional Population Growth and Distribution* (University of California Press, Berkeley, 1968).

# Terrain, Traffic and Tundra

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**The heavy vehicles of the oilmen roam widely over Northern Canada, leaving trails gouged out of the virgin tundra. The damage they inflict on the vegetation may mark them as a basic problem in the conservation of the Arctic.**

THE search for, and discovery of, oil and natural gas on the Arctic slope of North America epitomize the concept of wilderness and plenty, the subject of the 1969 Reith Lectures<sup>1</sup>. Conservation, that is the sensible use of all natural resources, demands that the oil and gas fields must be developed but that the wilderness be left unharmed.

One of the chief problems in this context is transport. Harbours, airports and depots are the focal point for all operations, and often bring about total destruction of the tundra ecosystem. The area affected in this way is very small, but from these points of focus, seismic trails, trackways and pipelines radiate, dissecting large areas of otherwise virgin tundra. Permanent roads mean permanent damage, but again these are few, most of the far ranging work being carried out by off-road vehicles. Each of these creates its own type of scars, which, given time, should heal; but how serious is the

damage they cause, and what is the time scale of regeneration? This article presents the results of a study, carried out in the Mackenzie Delta region of Canada, on the effect of off-road vehicular traffic.

## Terrain Characteristics and Damage

The floristic analysis of the twelve study sites is presented in Table 1. The sites were selected as representative of the main community types within the area, by reference to aerial photographs (scale, approximately 1:50,000). In the table the sites are arranged in order of a subjective gradient of "wetness"; the chief trend of variation within the vegetation (left to right in the table) correlates with an increase in the amount of free drainage. This increase causes drying out of the active (above permafrost) layer and a decrease in the relative throughput of ground water.

Airform pattern affords a direct insight into the problem, allowing the primary terrain features such as drainage axes, break of slope, patterned muskeg, polygons and so on, to be recognized and mapped<sup>2</sup>. Survey from lower altitudes (below 1,000 feet) enables recognition of the elements of secondary terrain structure, for example, mounds, hummocks and tussocks, most of which are products of biotic development. The full appreciation of the relationship is completed by studying the vegetation on the ground, either by applying the full phytosociological treatment<sup>3</sup> as in Table 1, or by adopting

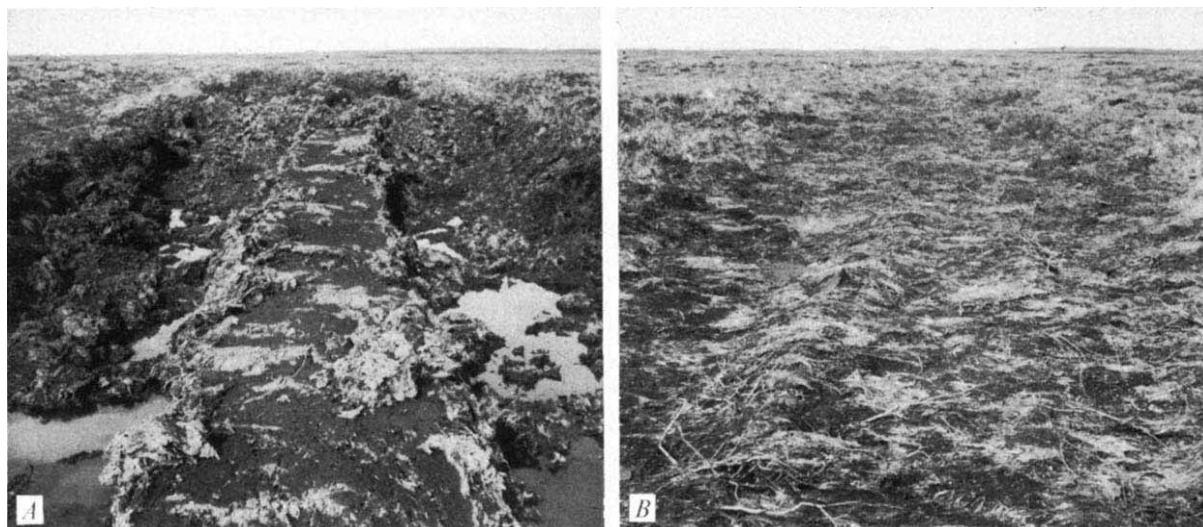


Fig. 1 Comparison of terrain damage caused by: A, twenty passes of a tracked vehicle (weight 120,000 pounds); B, 100 passes of a vehicle fitted with pliable rollers (weight, 17,000 pounds).



**Table 1** Floristic Analysis of the Vegetation of the Twelve Test Sites

| Area/site code<br>Radforth vegetation type <sup>4</sup><br>Gradient %<br>Comparable Alaskan<br>vegetation type <sup>5</sup> | Waterlogged → Free draining |                |               |               |                |                |                |                  |                |                |                |                | Percentage importance<br>value to natural<br>regeneration |
|-----------------------------------------------------------------------------------------------------------------------------|-----------------------------|----------------|---------------|---------------|----------------|----------------|----------------|------------------|----------------|----------------|----------------|----------------|-----------------------------------------------------------|
|                                                                                                                             | A1<br>FI<br>0               | A2a<br>FI<br>0 | B3<br>FI<br>0 | A2<br>FI<br>0 | A4<br>FEI<br>0 | A3<br>EFI<br>2 | C1<br>FEI<br>0 | B4<br>DEI<br>4.5 | B2<br>EFI<br>1 | B1<br>EFI<br>0 | C3<br>EFI<br>2 | C2<br>EI<br>10 |                                                           |
| <i>Sphagnum warnstorffianum</i>                                                                                             | 1,2                         | *              |               |               |                |                |                |                  |                |                |                |                |                                                           |
| <i>S. subsecundum</i>                                                                                                       | 3,3                         | 3,3            |               |               |                |                |                |                  |                |                |                |                |                                                           |
| <i>Meesia triquetra</i>                                                                                                     | +2                          | *              | 1,2           |               |                |                |                |                  |                |                |                |                |                                                           |
| <i>Scorpidium scorpioides</i>                                                                                               | +2                          | *              | 4,5           |               |                |                |                |                  |                |                |                |                |                                                           |
| <i>Carex aquatilis</i>                                                                                                      | 3,3                         | 2,1            | 1,1           |               |                |                |                |                  |                |                |                |                | 15                                                        |
| <i>Utricularia intermedia</i>                                                                                               | +1                          |                | +1            |               |                |                |                |                  |                |                |                |                | 0.5                                                       |
| <i>Potentilla palustris</i>                                                                                                 |                             |                | 1,2           |               |                |                |                |                  |                |                |                |                |                                                           |
| <i>Cinclidium stygium</i>                                                                                                   |                             |                | 1,2           |               |                |                |                |                  |                |                |                |                | 2                                                         |
| <i>Drepanocladus revolvens</i>                                                                                              |                             |                | 2,2           |               |                |                |                |                  |                |                |                |                |                                                           |
| <i>Scorpidium turgescens</i>                                                                                                |                             |                | 1,1           |               |                |                |                |                  |                |                |                |                |                                                           |
| <i>Eriophorum vaginatum</i>                                                                                                 | 1,1                         | +1             | 3,2           | 3,2           | *              | 2,2            | *              | *                | 1,2            | 1,2            | +2             |                | 0.5                                                       |
| <i>Sphagnum fuscum</i>                                                                                                      |                             |                | 1,2           | 4,3           | *              |                |                |                  |                |                |                |                |                                                           |
| <i>Polygonum bistorta</i> ssp. <i>plumosum</i>                                                                              |                             |                | +1            |               | *              | +1             | +1             |                  | *              | +1             |                |                | 3                                                         |
| <i>Rubus chamaemorus</i>                                                                                                    |                             |                | 1,1           | 1,1           | 1,1            |                |                |                  | *              |                |                | 1,1            | 11                                                        |
| <i>Ledum palustre</i> ssp. <i>decumbens</i>                                                                                 |                             |                | 2,1           | 1,1           | 1,2            | +1             | 2,2            |                  | 2,1            | 1,1            | 2,1            |                | 1                                                         |
| <i>Cetraria cucullata</i>                                                                                                   |                             |                | +2            | +1            | 1,1            | +1             | *              | +1               |                | +1             | +1             |                | 1                                                         |
| <i>Aulacomnium turgidum</i>                                                                                                 |                             |                | 1,2           | +1            | 1,2            | 2,2            | 1,2            | 1,2              | 1,2            | 3,3            | 2,3            |                | 14                                                        |
| <i>Betula nana</i> /glandulosa                                                                                              |                             |                | 1,1           | +1            | 1,2            | +1             | 2,3            | 2,2              | 1,1            | *              | 1,1            |                | 1                                                         |
| <i>Vaccinium uliginosum</i> ssp. <i>alpinum</i>                                                                             |                             |                | +2            | 2,3           | 1,1            | 2,2            | 2,3            | 1,2              | 2,1            | 1,1            |                |                | 3                                                         |
| <i>V. vitis idaea</i> var. <i>minus</i>                                                                                     |                             |                | 1,1           | 2,3           | 1,1            | +2             |                | 1,2              | +2             | 1,1            |                |                | 2                                                         |
| <i>Carex bigelowii</i>                                                                                                      |                             |                | +1            | 1,1           | 2,2            | 1,2            | 1,2            | 1,2              | 2,1            | 2,2            |                |                | 15                                                        |
| <i>Camptothecium nitens</i>                                                                                                 |                             |                |               |               | +2             | 1,2            | 1,2            | 2,3              | 1,2            | +1             | 1,2            |                | 13                                                        |
| <i>Arctostaphylos alpina</i> /rubra                                                                                         |                             |                |               |               | 3,3            | 2,3            | 1,2            | 2,3              | +2             | +2             | +2             |                | 3                                                         |
| <i>Petasites frigidus</i>                                                                                                   |                             |                |               |               | 1,1            | *              | +2             | 1,1              | +2             | +1             | +2             |                | 3                                                         |
| <i>Lupinus arcticus</i>                                                                                                     |                             |                |               |               | +1             | *              | +1             | +2               | +1             | +1             | +1             |                |                                                           |
| <i>Empetrum nigrum</i>                                                                                                      |                             |                |               |               | +1             | 2,3            | +1             | *                | +2             | 2,1            | 2,1            |                |                                                           |
| <i>Salix glauca</i>                                                                                                         |                             |                |               |               |                | +1             | 1,2            | 1,1              | 1,1            | 1,1            | +2             |                | 2                                                         |
| <i>Dryas octopetala</i> /integrifolia                                                                                       |                             |                |               |               |                |                | +1             | 1,1              | 1,1            | +1             | 1,1            |                | 2                                                         |
| <i>Alnus crispa</i>                                                                                                         |                             |                |               |               |                |                |                | 1,2              | +2             |                | 1,2            |                |                                                           |
| <i>Icmaophila ericetorum</i>                                                                                                |                             |                |               | 1,2           |                |                |                |                  |                |                |                |                |                                                           |
| <i>Equisetum arvense</i>                                                                                                    |                             |                |               |               |                |                |                | +1               |                |                |                |                | 1                                                         |
| <i>Arctagrostis latifolia</i>                                                                                               |                             |                |               |               |                |                |                |                  | +1             |                | +2             |                | 1                                                         |
| <i>Eriophorum angustifolium</i> /russeolum                                                                                  |                             | *              | 1,1           |               |                |                | +1             |                  |                |                |                |                |                                                           |
| <i>Carex</i> ssp. seedlings                                                                                                 |                             |                |               |               |                |                |                |                  |                |                |                |                | 6                                                         |
| Total positive records of regeneration, 468 = 100                                                                           |                             |                |               |               |                |                |                |                  |                |                |                |                |                                                           |

Only the more important members of the vegetation are included in the table. The first figure or symbol in each column is a subjective estimate<sup>2</sup> of cover abundance, and the second, a subjective index of sociability<sup>3</sup>. An asterisk in a column indicates that the species was present in the vegetation but not in the quadrat studied. The last column indicates the importance of each species in short term regeneration; this is expressed as a percentage of the total number of positive records of regeneration in the ruts studied.

Area codes: A, Shingle Point; B, Tununuk; C, Tuktoyaktuk.

Comparable Alaskan vegetation types: 1, *Eriophorum*/ *Carex* wet meadow; 2, *Eriophorum* tussock; 3, *Carex bigelowii* high centre polygon; 4, *Dryas* fell field (see ref. 5).

the Radforth muskeg classification system<sup>4</sup> which is based on physiognomic characteristics (Table 2).

The floristic composition of an area undoubtedly exerts a strong influence on its potentiality for regeneration. The secondary terrain structure affects trafficability, and also its destruction has a great effect on the pattern and speed of regeneration. All these factors must therefore be considered when investigating the disturbance caused by off-road vehicles.

The results of tests on all sites using one type of tracked vehicle (weight, 8,500 pounds) are presented in Table 3. It is at once obvious that the severity of damage is related to "wetness" of the terrain and therefore to the type of vegetation. Three main processes of damage may be recognized: (a) the destruction of the living vegetation; (b) the destruction of the secondary terrain structure; (c) the production of ruts which destroy the active layer and expose the permafrost to solar radiation; this results in thawing and slumping which, in turn, can be expected to lead to erosion in sloping areas. All

three processes take place simultaneously, though (a) and (b) usually progress earlier than the effects of (c).

Cases of erosion, initiated by ruts, were, in fact, very few and were confined to areas where ice-wedged polygons on steep slopes were traversed. Even here, the effects were confined merely to localized slumping between the polygons. In areas like this, which are characterized by easily damaged but rapidly regenerating FI-type vegetation (see below), and by terrain which is normally under high stress during freezing and thawing, erosion effects would probably remain localized.

It would seem safe to postulate that the more advanced the process of destruction, the longer it will take for complete regeneration to occur.

## Rut Regeneration

The first series of tests were made on June 22, 1970, and each area was tested to maximum destruction (8.8 on the scale). Regeneration was studied two months later. All ruts exhibited

regeneration, measured as the percentage number of random 1 cm squares containing new growth, ranging from 2% to 56%. A total of twenty species was recorded. Only three of the flowering plants were found in the form of seedlings, the rest having developed from vegetative propagules left in the rut. There was no correlation between the success of this short term regeneration and the type of vehicle used or the

type of vegetation destroyed. The relative importance of each species recorded during these short term regeneration studies is indicated in the last column of Table 1.

The study of old tracks in the Mackenzie Delta and also around Churchill in northern Manitoba revealed, without doubt, that long term regeneration is more efficient in the most poorly drained vegetation types, that is those corresponding to A1, A2 and B3 (Table 1). In most cases, ruts more than 5 yr old had disappeared in the FI vegetation of watertracks and around standing water. In contrast, ruts in EH vegetation of high centre polygons and palsas (for example, marbled airform pattern<sup>6</sup>) were still obvious both from the air and on the ground although they were more than 20 yr old. Even in these cases, however, a full complement of species was present, all of which were producing organs of reproduction. Where tracks passed through taiga forest and scrub (where a scar is naturally more obvious, both from the air and on the ground), again, in most cases, young trees were abundant.

### Types of Vehicle

Whatever the rate of recovery, it is important to discover ways of reducing the amount of damage caused by a given task. To this end, tests were carried out on three sites with five vehicles of different weights. Three of them were fitted with conventional tracks with grouser bars, one with cleated tyres and one with smooth pliable rollers. The results of the

**Table 2** Radforth Classification System for Muskeg Vegetational Types<sup>4</sup>

| Cover class | Description                                          |
|-------------|------------------------------------------------------|
| A           | Trees over 15 feet high                              |
| B           | Trees up to 15 feet high                             |
| C           | Non-woody, grass-like 2-5 feet high                  |
| D           | Woody, tall shrubs or dwarf trees 2-5 feet high      |
| E           | Woody shrubs up to 2 feet high                       |
| F           | Sedges and grasses up to 2 feet high                 |
| G           | Non-woody broad-leaf plants up to 2 feet high        |
| H           | Leathery to crisp mats of lichen up to 4 inches high |
| I           | Soft mats of moss up to 4 inches high                |

Nine basic structural vegetational types are recognized, each designated by a letter of the alphabet. By using only those vegetational types having more than 25% total cover, vegetation can be described by sets of up to three letters.

**Table 3** Results of Terrain Damage Tests on all Sites using one Vehicle

| No. of passes | Waterlogged    |     |     |     |     | Free-draining |     |     |     |     |     |     |  |
|---------------|----------------|-----|-----|-----|-----|---------------|-----|-----|-----|-----|-----|-----|--|
|               | Area/site code |     |     |     |     |               |     |     |     |     |     |     |  |
|               | A1             | A2a | B3  | A2  | A4  | A3            | C1  | B4  | B2  | B1  | C3  | C2  |  |
| 100           | 8,8            | 8,8 | 8,6 | 8,8 | 8,8 | 8,8           | 8,7 | 8,8 | 8,7 | 8,8 | 7,7 | 6,7 |  |
| 80            | 8,8            | 8,8 | 8,6 | 8,8 | 8,7 | 8,8           | 7,7 | 8,8 | NR  | 8,7 | 6,6 | 6,7 |  |
| 60            | 8,8            | 8,8 | 8,6 | 8,7 | 7,7 | 8,7           | 7,7 | 7,8 | 7,7 | 6,7 | 6,5 | 5,5 |  |
| 40            | 8,8            | NR  | 6,4 | 7,7 | 6,5 | 7,7           | 6,5 | 5,7 | 5,6 | 5,6 | 5,4 | 5,4 |  |
| 20            | 8,8            | 7,6 | 5,3 | 6,5 | 5,4 | 4,7           | 6,4 | 4,5 | 3,4 | NR  | 4,3 | 5,3 |  |
| 10            | 8,7            | 6,6 | 4,2 | 2,3 | 4,3 | 3,6           | 5,3 | 4,4 | 3,3 | NR  | 2,3 | 3,3 |  |
| 5             | 7,7            | 6,6 | 3,1 | 2,2 | 3,3 | 2,5           | 4,2 | 3,3 | 2,2 | NR  | 2,2 | 2,2 |  |
| 1             | 7,6            | NR  | 3,1 | 2,1 | 2,3 | 2,5           | 1,1 | 1,2 | NR  | NR  | 1,1 | 1,1 |  |

The vehicle was fitted with conventional tracks with grouser bars, and weighed 8,500 pounds.

Damage is assessed on a two-figure, eight-point scale, the first figure being a subjective estimate of destruction of the secondary terrain structure, and the second, an estimate of damage to the living mat of vegetation.

NR, not recorded.

**Table 4** Results of Terrain Damage Tests carried out on Three Sites in the Tuktoyaktuk (C) Test Area, using Six Vehicle Load Systems

| No. of passes              | Area/site code                        |     |     |                                      |     |     |                                |     |     |                                     |     |     |                                                   |     |     |     |
|----------------------------|---------------------------------------|-----|-----|--------------------------------------|-----|-----|--------------------------------|-----|-----|-------------------------------------|-----|-----|---------------------------------------------------|-----|-----|-----|
|                            | C1                                    | C3  | C2  | C1                                   | C3  | C2  | C1                             | C3  | C2  | C1                                  | C3  | C2  | C3                                                | C3  | C1  | C2  |
| 100                        | 8,8                                   | 8,8 | 8,8 | 8,8                                  | 8,8 | 8,7 | 8,7                            | 8,8 | 8,7 | 8,7                                 | 7,8 | 7,8 | 6,6                                               | 6,7 | 6,6 | 6,6 |
| 80                         | 8,8                                   | 8,8 | 8,8 | 8,8                                  | 8,7 | 7,6 | 8,7                            | 8,7 | 6,4 | 7,7                                 | 6,6 | 6,7 | 6,3                                               | 6,4 | 5,5 | 5,5 |
| 60                         | 8,8                                   | 8,8 | 8,8 | 8,8                                  | 7,6 | 6,5 | 7,7                            | 6,6 | 6,4 | 6,5                                 | 6,5 | 5,5 | 6,3                                               | 6,4 | 4,4 | 4,4 |
| 40                         | 8,8                                   | 8,8 | 8,8 | 7,6                                  | 7,5 | 6,5 | 6,6                            | 6,5 | 4,4 | 6,4                                 | 5,4 | 5,4 | 5,3                                               | 4,3 | 4,4 | 3,3 |
| 20                         | 8,8                                   | 8,8 | 7,7 | 6,5                                  | 6,4 | 5,4 | 5,3                            | 4,4 | 3,4 | 5,3                                 | 4,3 | 5,3 | 4,3                                               | 4,3 | 4,3 | 2,3 |
| 10                         | 7,7                                   | 7,7 | 6,5 | 4,5                                  | 5,3 | 5,3 | 5,3                            | 4,3 | 3,3 | 5,3                                 | 2,3 | 3,3 | 4,3                                               | 4,3 | 4,3 | 2,2 |
| 5                          | 7,6                                   | 6,7 | 5,3 | 4,4                                  | 4,2 | 3,3 | 3,2                            | 3,3 | 2,2 | 4,2                                 | 2,2 | 2,2 | 2,2                                               | 3,2 | 3,3 | 1,2 |
| 1                          | 5,4                                   | 5,5 | 4,2 | 2,1                                  | 2,1 | 2,1 | 1,1                            | 1,1 | 1,1 | 1,1                                 | 1,1 | 1,1 | 1,1                                               | 1,1 | 1,1 | 1,1 |
| Type and weight of vehicle | Track with grouser bars<br>120,000 lb |     |     | Track with grouser bars<br>46,000 lb |     |     | Tyres with cleats<br>15,400 lb |     |     | Track with grouser bars<br>9,000 lb |     |     | Smooth pliable roller<br>20,000 lb      17,000 lb |     |     |     |

For method of damage assessment see Table 3. The tests were carried out in late June 1970. The lines across column groups relate to the number of passes required of the different vehicles to deliver the same weight load; their position is determined using calculations based on the vehicles' gross weights.



multi-pass tests are given in Table 4. In all cases each vehicle exhibited differential effects between sites, and, except the vehicle with the smooth rollers, all elicited the same differential response. The wettest terrain sustained the greatest damage and the well-drained site on a 10% slope was the least affected. Comparison between vehicles indicates that the damage decreases with the decreasing weight of the vehicle. Again the only exception to this was the vehicle with the smooth traction surface. The results of tests with this vehicle indicate that future engineering effort might be directed towards further development of tracks that are flat or that conform to the surface contours of the secondary terrain, thereby spreading the highspot loading.

More extensive work (especially between seasons) is necessary, but probably a meaningful task-damage scale could easily be prepared, enabling work to be planned on a "minimum terrain disturbance" basis by using a vehicle system appropriate to the task in hand. The maximum number of passes which would cause no more than an allowed level of disturbance could also be established. Projects could be planned to this end simply by using air photographs backed by the Radforth classification system on the ground. It is known that the latter can be easily understood and applied by

vehicle operators. Establishing "acceptable" levels of terrain disturbance, however, would be a necessary preliminary to such planning procedures.

Further biological work should aim to ascertain the full ecological impact of these types of terrain disturbance, and to investigate more fully the process of regeneration. Until adequate knowledge of the latter is gained, the seeding of ruts with plants, however well suited to the environment they may be, could turn what are, in the time scale of the tundra, ephemeral scars into permanent biotic features.

Received March 4; revised April 13, 1971.

- <sup>1</sup> Fraser Darling, F., *Wilderness and Plenty* (BBC, London, 1970).
- <sup>2</sup> Radforth, N. W., *Organic Terrain Organization from the Air* (Handbook No. 2, Defense Research Board, Dept. Nat. Defense, DR No. 124, Ottawa, 1958).
- <sup>3</sup> Braun Blanquet, J., *Pflanzensoziologie*, 865 (Springer, Wien, 1964).
- <sup>4</sup> Radforth, N. W., in *Muskeg Engineering Handbook* (edit. by MacFarlane, I. V.) (University of Toronto Press, 1969).
- <sup>5</sup> Johnson, A. W., Viereck, L. A., Johnson, R. E., and Melchoir, H., in *The Environment of Cape Thompson Region Alaska*, 277 (US Atomic Energy Commission, 1965).
- <sup>6</sup> Korpilaakko, E. O., and Radforth, N. W., *Proc. 3rd Int. Peat Cong. Quebec*, 69 (Runge Press, 1968).

# Sex Determination in Birds and Mammals

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**The Y chromosome of higher vertebrates may exert its influence by regulating the growth rate of the gonadal rudiment. It seems that the faster growing rudiment differentiates into a testis in mammals and an ovary in birds.**

ONE of the puzzling aspects of the genetics of sex determination is the apparently haphazard distribution of sex chromosomes between the sexes in different classes of animals. In mammals, including man, the male is heterogametic, having an X and a Y chromosome, and the female has two X chromosomes. In birds, however, and in those reptiles which have been examined so far, the situation is reversed, the female being the heterogametic and the male the homogametic sex; in amphibia and in fish, both systems are found<sup>1-3</sup>. Among insects, the male is heterogametic in the Diptera and Orthoptera, but in the Lepidoptera, males are homogametic and females heterogametic<sup>4</sup>.

## Gonadal Rudiment Growth

The exact manner in which the sex chromosomes determine sex is not yet known for any group. In mammals, however, the combined cytogenetic and embryological evidence suggests that the Y chromosome causes the gonadal rudiment to develop into a testis, which in turn is responsible for the subsequent differentiation of the male phenotype<sup>5,6</sup>. During the early stages of gonadal differentiation, the incipient mammalian testis is larger than the incipient ovary<sup>7-9</sup>. It has been suggested that the mammalian Y chromosome may increase the rate

of growth of the gonadal rudiment, which may need to reach a critical size by a given stage of development in order to become a testis; if it fails to reach the required size, the gonad develops into an ovary<sup>8,9</sup>.

In evaluating this interpretation, the corresponding situation in birds is clearly of special relevance. Results obtained so far<sup>10</sup> suggest that during early sex differentiation in chick (*Gallus domesticus*) embryos, the left ovary (which is the only one to develop) grows faster than the male gonads. The results are still preliminary and some important details remain to be worked out. This applies particularly to a comparison of growth rates in terms of cell number and cell turnover, and also to a more precise determination of the time at which the increased growth rate of the female gonad begins in relation to other aspects of gonadal differentiation. Nevertheless, the results obtained by measuring gonadal volumes provide *prima facie* evidence that during the early stages of gonadal sex differentiation in birds, the ovary grows faster than the testis. The situation is therefore the opposite to that found in mammals, and therefore reflects the sex chromosome constitution.

In animals with female heterogamety, many authors refer to the chromosome which is present only in females as W and the paired sex chromosomes of males as ZZ. As long ago as 1933, however, Winge<sup>11</sup> proposed that the simpler XY terminology be used throughout, and this proposal will be followed here.

## Bird Sex

Whereas in mammals there is much evidence for the male determining capacity of the Y chromosome, it has not yet been established that the Y chromosome of birds is female determining. This is because diploid birds with XXY or with XO sex chromosomes have not yet been described. Triploid chickens with XXY sex chromosomes, however, have intersexual phenotypes (ref. 12 and S. E. Bloom, personal communication).

This observation is compatible with the tentative assumption that the *Y* chromosome of birds is female determining, though its power in this respect may be less strong than the male determining capacity of the mammalian *Y* chromosome. One may further postulate that the function of the avian *Y* chromosome may be to increase the rate of growth of the left gonadal rudiment, and that this rudiment, if it reaches a certain size by a given stage of development, becomes an ovary. If it fails to reach this size it develops into a testis. The right gonad of female birds usually cannot differentiate into an ovary and normally remains in a rudimentary state of development<sup>13-15</sup>. If the left ovary is removed or diseased, however, the right gonad may resume growth and typically develops into a testis, which sometimes produces sperm. Occasionally, an ovotestis may be formed.

Experiments in which early embryos were castrated have demonstrated another difference in the mode of sex differentiation in birds and mammals. Jost<sup>16</sup> has shown that in mammals, embryonic testes are necessary for the differentiation of the male phenotype; if the gonads are removed, the embryos develop an essentially female phenotype whatever their sex chromosome constitution. The corresponding avian work was carried out by Wolff and Wolff<sup>17</sup> who succeeded in castrating embryos of birds using X-rays. Fully castrated embryos of the duck and the fowl had a preponderantly male type morphology and the authors concluded that an ovarian hormone was required to prevent the development of the male secondary sexual characters. As well as a male type syrinx and penis, however, castrated chick embryos had two oviducts, whereas normal males have none and normal females have only the left one. These experiments suggest that in birds, the ovary is the dominant embryonic gonad. This contrasts with the situation in mammals, in which the testis is the dominant embryonic gonad. These findings reinforce the apparently paradoxical suggestion that sex differentiation might be associated with additional growth of the ovarian rudiment in birds and of the testicular rudiments in mammals.

## Possible Mechanisms

It is not yet possible to say what causes the additional growth of the respective gonadal rudiments. In mammals, the *Y* chromosome is undoubtedly implicated and it has been suggested that at the chromosomal level, the situation may be analogous with that in *Drosophila*. In several species of *Drosophila*, the *Y* chromosome ensures the motility of the sperm and also affects its length. It has been demonstrated that the *Y* chromosome forms evanescent lampbrush-like loops which are active in RNA synthesis in the spermatocytes of male larvae<sup>18</sup>. One might postulate that during certain stages of development, the *Y* chromosome of vertebrates may also contain sites which are particularly active in RNA synthesis; these may be situated in cells of the gonadal rudiment and may stimulate mitotic divisions.

The sexes differ not only in the presence or absence of a *Y* chromosome, but also in the number of *X* chromosomes. It has been postulated that different chromosome constitutions may have a direct effect on rates of cell proliferation<sup>4,6,9,19-23</sup>. A possible mechanism for this is suggested by observations on plants in which it has been discovered that the presence of supernumerary *B* chromosomes may increase the length of the mitotic cycle<sup>24</sup>, and that in some species the time required for DNA synthesis is proportional to the amount of DNA per nucleus<sup>25</sup>. Recent confirmation of this idea has been obtained from investigations on human cells. Kaback and Bernstein<sup>26</sup> found that in fibroblasts of patients with mongolism, the rate of DNA synthesis was slowed down, thus supporting earlier preliminary evidence<sup>23</sup>. Further confirmation is given by the work of Mellman *et al.*<sup>27</sup> who reported that in cultures of lymphocytes from mongols, the maximum rate of DNA synthesis was below that of controls, and Polani<sup>28</sup> mentioned that in *XO* (45, *X*) cells the length of the mitotic cycle was consider-

ably shorter than in normal male and female cells. These findings provide strong evidence that abnormalities due to aneuploidy may be caused by differences in the rates of cell proliferation during embryonic development. By implication, the same may be true of developmental differences associated with the normal sex chromosome dimorphism<sup>6</sup>. If a particular chromosome shows specific activity in certain cells during development, its presence or absence might be expected to lead to differential growth of these cells.

The process of sex determination by means of gonadal differentiation may therefore take place in the following way. Originally, the gonadal rudiment is bipotential, its ultimate course of development depending on the rate of growth at a given stage of development. If a *Y* chromosome is present, it may speed up the rate of growth of the gonadal rudiment, which, as a result, develops into the dominant gonad of the heterogametic sex, namely the testis in mammals and the ovary in birds. In the absence of a *Y* chromosome, the gonadal rudiment grows more slowly into the embryonically less powerful gonad of the homogametic sex, namely, the ovary of mammals and the testis of birds.

## Hormonal Influence

The difference in the gonadal differentiation of birds and mammals may be correlated with differences in their reproductive physiology. The mammalian embryo develops inside the mother, and even though only a small quantity of the female sex hormones may traverse the placenta and enter the embryo<sup>29</sup>, embryos of both sexes are nonetheless exposed to them<sup>30</sup>. A male embryo, therefore, may have to overcome these by means of its own gonadal secretions. If the *Y* chromosome does, indeed, speed up the growth and development of the gonadal rudiments, it may need to be present in the male during the period of its competitive struggle for hormonal supremacy. In contrast, the avian embryo is removed from its mother's sphere of influence long before its sexual development is threatened. The embryonic testes are required only for the relatively minor task of causing the Mullerian ducts to regress. The major task of sexual differentiation of the embryo, however, devolves on the ovary, whose extra growth at this stage might be of advantage in preparing it for its ultimately more demanding role of egg production.

## Evolving Sex

Although highly developed sex chromosomes are a feature of birds and mammals, in many lower vertebrates there are no morphologically distinguishable sex chromosomes. In some lower vertebrates, sex can be determined by environmental agents such as temperature<sup>31,32</sup>. The demonstration by Ohno *et al.*<sup>33</sup> that the evolution of the vertebrates has been accompanied by a repeated increase in the chromosomal material may be of special relevance in this connexion. The authors propose that the significance of this increase was the resulting duplication of specific gene loci, but it is quite possible that an even more important function of the additional chromosomes and chromosomal regions was to enlarge the mechanism controlling the rate of cell proliferation during development. In particular, the sex chromosomes of birds and mammals may be regarded as having arisen from ordinary chromosomes<sup>34,35</sup>, some of whose gene loci may no longer have been required for their original purpose. These subsequently took over the function of regulating the growth of the gonadal rudiments independently of environmental conditions.

The mechanism by which phenotypic effects, originally induced by environmental stimuli, have been taken over by the genetic material, has been called "genetic assimilation" by Waddington<sup>36,37</sup>. It may be that the evolution of sex chromosomes provides an outstanding example of this.

There are several aspects of this hypothesis which can be tested by experiment. They open up the possibility of a new developmental cytogenetics, in which differences in phenotypes



associated with differences in chromosomal constitutions may be traced back to differences in rates of cell proliferation.

I thank Dr S. E. Bloom for discussions. This work was supported by a grant from the Science Research Council.

Received January 23, 1971.

- <sup>1</sup> Beatty, R. A., in *Intersexuality* (edit. by Armstrong, C. N., and Marshall, A. J.), 17 (Academic Press, London and New York, 1964).
- <sup>2</sup> Beatty, R. A., *Phil. Trans. Roy. Soc., B*, **259**, 3 (1970).
- <sup>3</sup> Bianchi, N. O., Beçak, W., de Bianchi, M. S. A., Beçak, M. L., and Rabello, M. N., *Chromosoma*, **26**, 188 (1969).
- <sup>4</sup> Mittwoch, U., *Sex Chromosomes* (Academic Press, New York and London, 1967).
- <sup>5</sup> Hamerton, J. L., *Nature*, **219**, 910 (1968).
- <sup>6</sup> Mittwoch, U., *Nature*, **221**, 446 (1969).
- <sup>7</sup> Lindh, J., *Quantitative Aspects of Prenatal Growth in Albino Rat and Golden Hamster studied by Morphologic and Experimental Methods* (Department of Anatomy, Lund, 1961).
- <sup>8</sup> Mittwoch, U., Delhanty, J. D. A., and Beck, F., *Nature*, **224**, 1323 (1969).
- <sup>9</sup> Mittwoch, U., *Phil. Trans. Roy. Soc., B*, **259**, 113 (1970).
- <sup>10</sup> Mittwoch, U., Narayanan, T. L., Delhanty, J. D. A., and Smith, C. A. B., *Nature New Biology*, **23**, 197 (1971).
- <sup>11</sup> Winge, O., *Proc. Sixth Intern. Cong. Genet.*, 343 (1932).
- <sup>12</sup> Ohno, S., Kittrell, W. A., Christian, L. C., Stenius, C., and Witt, G. A., *Cytogenetics*, **2**, 42 (1963).
- <sup>13</sup> Lillie, F. R., *Development of the Chick*, third ed. (revised by Hamilton, H. L.) (Henry Holt, New York, 1952).
- <sup>14</sup> Romanoff, A. L., *The Avian Embryo* (Macmillan, New York, 1960).
- <sup>15</sup> Crew, F. A. E., *Sex Determination*, fourth ed. (Methuen, London, 1965).
- <sup>16</sup> Jost, A., *Phil. Trans. Roy. Soc., B*, **259**, 119 (1970).
- <sup>17</sup> Wolff, Et., and Wolff, Em., *J. Exp. Zool.*, **116**, 59 (1951).
- <sup>18</sup> Hess, O., *Mol. Gen. Genetics*, **106**, 328 (1970).
- <sup>19</sup> Mittwoch, U., *Nature*, **204**, 1032 (1964).
- <sup>20</sup> Mittwoch, U., *Nature*, **214**, 554 (1967).
- <sup>21</sup> Mittwoch, U., *Nature*, **219**, 1074 (1968).
- <sup>22</sup> Mittwoch, U., *Bull. Europ. Soc. Human Genet.*, **4**, 6 (1970).
- <sup>23</sup> Mittwoch, U., in *Mongolism* (edit. by Wolstenholme, G. E. W., and Porter, R.), 51 (Churchill, London, 1967).
- <sup>24</sup> Ayonoadu, U. W., and Rees, H., *Exp. Cell Res.*, **52**, 284 (1968).
- <sup>25</sup> Van't Hof, J., *Exp. Cell Res.*, **39**, 48 (1965).
- <sup>26</sup> Kaback, M. M., and Bernstein, L. H., *Ann. NY Acad. Sci.*, **171**, 526 (1970).
- <sup>27</sup> Mellman, W. J., Younkin, L. H., and Baker, D., *Ann. NY Acad. Sci.*, **171**, 537 (1970).
- <sup>28</sup> Polani, P. E., *Proc. Roy. Soc. Med.*, **63**, 955 (1970).
- <sup>29</sup> Diczfalusy, E., and Mancuso, S., in *Foetus and Placenta* (edit. by Kloppe, A., and Diczfalusy, E.), 191 (Blackwell, Oxford and Edinburgh, 1969).
- <sup>30</sup> Goss, R. J., *Adaptive Growth*, 251 (Logos Press, London, 1964).
- <sup>31</sup> Witschi, E., *Biol. Symp.*, **6**, 51 (1942).
- <sup>32</sup> Harrington, R. W., *Physiol. Zool.*, **41**, 447 (1968).
- <sup>33</sup> Ohno, S., Wolf, U., and Atkin, N. B., *Hereditas*, **59**, 169 (1968).
- <sup>34</sup> Darlington, C. D., *Evolution of Genetic Systems* (Oliver and Boyd, Edinburgh and London, 1958).
- <sup>35</sup> Ohno, S., *Sex Chromosomes and Sex-linked Genes* (Springer, Berlin, Heidelberg, New York, 1967).
- <sup>36</sup> Waddington, C. H., *The Strategy of the Genes* (George Allen and Unwin, London, 1957).
- <sup>37</sup> Waddington, C. H., in *Towards a Theoretical Biology* (edit. by Waddington, C. H.), **1**, *Prologomena*, 1 (Edinburgh University Press, 1968).

# Role of Electrical Repulsive Forces in Synovial Fluid

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**Measurements suggest that electrical repulsive forces may be of significance in the boundary lubrication of surfaces by synovial fluid.**

SOLID surfaces often become electrically charged by the adsorption of ions when immersed in a polar liquid such as an aqueous electrolyte solution and the adsorbed ions attract ions of opposite sign in the liquid so as to establish a double layer of electric charge at the interface. If the double layers on neighbouring surfaces are similarly oriented, they give rise to electrical repulsive forces which can be directly and conveniently measured<sup>1,2</sup> by using the contact formed between a soft optically smooth rubber sphere<sup>3</sup> and a polished glass plate. Certain electrolyte solutions squeezed between these surfaces cannot be completely expressed; a thin equilibrium film of liquid is always maintained by double layer repulsion which supports the applied contact pressure when surfaces are a few hundred ångströms apart. The thickness of this film decreases with increasing contact pressure or increasing concentration of ions in the electrolyte solution provided the surface charge remains constant. Even when surfaces have been in static

contact for a considerable period of time a thin equilibrium film still separates them. This provides effective lubrication at any moment, should the surfaces be tangentially sheared.

## Equilibrium Film Thickness

Debate<sup>4</sup> surrounds the mechanism by which synovial fluid lubricates the cartilage surfaces of animal bone joints. It is known<sup>5,6</sup>, for example, that it is relatively ineffective as a lubricant between hard surfaces, such as metals. This may well be due to the high local contact pressures which occur between metals. By contrast, contact pressures generated when surfaces of rubber and glass are pressed together are of the same order of magnitude as those encountered in bone joints (about 1–10 atm.). For this reason experiments were carried out in which different specimens of synovial fluid taken from postmortem human knee joints were examined for their squeeze-film behaviour in our optical rubber–glass contact system. For this apparatus only 0.05 ml. of fluid was required per test. Six specimens were examined and in each case equilibrium films 100–300 Å thick—measured by a photometric technique<sup>7</sup>—were obtained in the contact after squeezing for 3–6 h. The results varied but the thickness of these films depended unmistakably on the applied contact pressure. If a film reached equilibrium under a constant contact pressure and the pressure

was then reduced, the film grew thick again until a new equilibrium was established. The detailed results in two extreme cases are shown in Fig. 1. One of these fluids was taken from a healthy joint, the other from an arthritic joint. In both cases, equilibrium films decreased in thickness with increasing contact pressure but the thickness of the arthritic fluid was decreased the most. Of the other cases examined, all produced equilibrium films intermediate in thickness between these two. Details concerning the six fluid specimens are shown in Table 1 and a complete summary of their equilibrium data is given in Fig. 2, but with point scatter omitted for clarity.

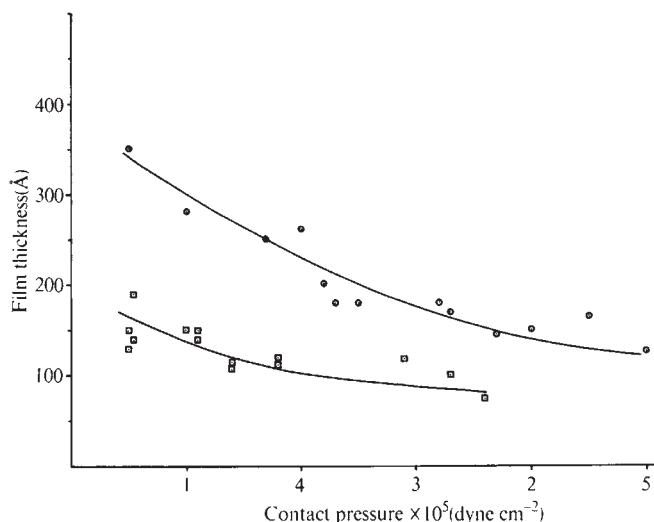


Fig. 1 Variation of film thickness with pressure for two extreme cases of synovial fluid.  $\circ$ , Results for normal fluid;  $\square$ , results for arthritic fluid.

Ogston and Stanier<sup>8</sup> found a similar equilibrium film behaviour when they compressed synovial fluid between glass surfaces, though they obtained films 200–500 Å thick at considerably higher contact pressures (10–100 atm.) than we have used. In this work it was suggested that the resistant film formed between surfaces was probably due mainly to mechanical support from hyaluronic acid molecules contained in the fluid. Our results, however, strongly suggest that a resistant equilibrium film is formed in synovial fluid by the action of electrical double layer repulsive forces which prevent the rubber and glass surfaces from coming into intimate contact. The results are in accord with published measurements<sup>2,9,10</sup> of the variation with distance of double layer repulsion, though the exact magnitude of the repulsive force seems to differ from fluid to fluid. This difference may have some bearing on the healthiness of each fluid. One other comment may be made about these results. The mucopolysaccharide, hyaluronic acid, contained in synovial fluid, is generally regarded as a straight chain polymer of molecular weight one million or more, coiled on itself and combined with protein in solution to form spherical or ellipsoidal networks about 0.5  $\mu\text{m}$  in diameter<sup>11–13</sup>. Yet when synovial fluid is squeezed between rubber and glass, films less than one-tenth of this diameter are formed. This may be because the hyaluronic acid molecules are squeezed out of the contact zone. Alternatively, they may be trapped and depressed into the soft rubber surface or squashed flat since they are flexible chain polymers with little rigidity. This suggests that the principal factor holding the rubber and glass surfaces apart is not mechanical but electrical: the surface charge is presumably acquired by the adsorption of small charged species, such as certain proteins, from the synovial plasma. We note with interest that measurements very recently published by Radin, Swann and Weissner<sup>14</sup> suggest that the joint lubricating fraction of bovine synovial fluid is a protein or glycoprotein free of hyaluronate.

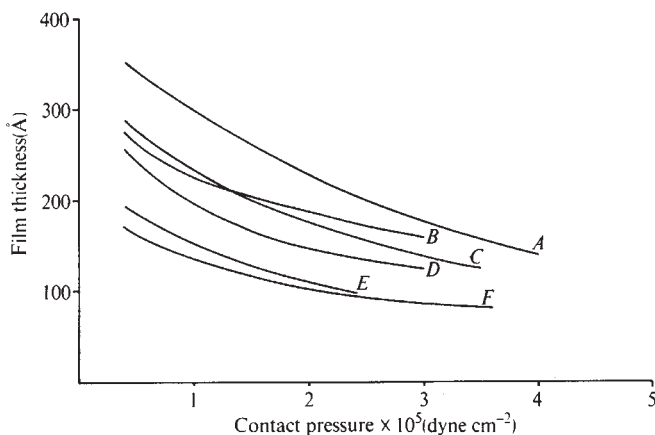


Fig. 2 Equilibrium film thickness data for six different specimens of synovial fluid. The specimens are identified in Table 1.

## Viscosity of Synovial Fluid Films

Unfortunately, our samples were too small for bulk viscosity measurements to be made, but thin film viscosity measurements of the six fluids could be made in the rubber-glass contact in two ways. First, the effective viscosity of films over a broad range of thickness was found by measuring the rate at which they thinned when squeezed between surfaces. Reynolds's equation<sup>15</sup> for the normal approach of parallel surfaces was used to calculate the squeeze film viscosity. Second, the viscosity of very thin films of equilibrium or near equilibrium thickness was found by measuring the frictional drag between contact surfaces when set in relative tangential motion. The equilibrium film viscosities were calculated from Newton's equation. It should be stressed that in the second method, calculations were based on instantaneous friction measurements. The frictional force between surfaces increased rapidly as tangential motion began but then quickly decreased to a smaller value as a relatively thick fluid film was formed. The peak instantaneous friction corresponds to the initial force required to shear the equilibrium film. The viscosity measurements gave considerably varying results, but within the range of reproducibility the viscosity did not vary greatly between healthy and osteo-arthritic fluids for film thicknesses ranging from 200 to 10,000 Å. The viscosity of thinner films tended to increase (Table 2). Generally the thin film values were larger than those usually obtained by bulk viscosity measurements.

## Effect of Sodium Chloride

If equilibrium films of synovial fluid are supported by double layer repulsion forces, some change in their thickness can be expected by increasing the number of ions present in the fluid. The effect of an ion increase in the arthritic fluid, F, was investigated by adding 50 mequiv./l. of solid sodium chloride. Equilibrium films increased in thickness and approached the values for fluid A taken from a healthy joint. It is not possible to state categorically that this implies a deficiency of sodium chloride in arthritic fluid, because although sodium chloride is the major electrolytic constituent of synovial fluid (~250 mequiv./l. in normal fluid) the actual amount varies from specimen to specimen<sup>16,17</sup>. Nevertheless, saline solution gives some reduction in stiffness and relief of pain in arthritic joints<sup>28</sup>.

## Equilibrium Films of Saliva

We have also attempted to determine whether other body lubricants such as saliva show double layer repulsion phenomena. Using the rubber-glass contact method, equilibrium films of saliva were formed 100–300 Å thick, the exact thickness



**Table 1** Details of Synovial Fluid Specimens

| Specimen                                                                                      | A                                   | B                                                  | C                             | D                                 | E                                 | F                                                                 |
|-----------------------------------------------------------------------------------------------|-------------------------------------|----------------------------------------------------|-------------------------------|-----------------------------------|-----------------------------------|-------------------------------------------------------------------|
| Age and sex of patient                                                                        | 60<br>F                             | 69<br>F                                            | 50<br>M                       | 66<br>M                           | 80<br>F                           | 74<br>M                                                           |
| Joint condition                                                                               | Normal                              | Normal                                             | Normal                        | Normal                            | Normal                            | Osteo-arthritic                                                   |
| Fluid colour                                                                                  | Pale straw                          | Colourless                                         | Straw                         | Straw                             | Yellow/green                      | Yellow/green                                                      |
| Fluid clarity                                                                                 | Clear                               | Some fine particles                                | Clear                         | Fairly clear                      | Cloudy                            | Very cloudy                                                       |
| Appearance of fluid under microscope when sandwiched in contact zone between rubber and glass | Uniform thin film. No cells visible | Uniform film disturbed at points by fine particles | Uniform film. No disturbances | Thin even film. No irregularities | Thin film disturbed by some cells | Cells and large gelatinous blobs greatly disturb evenness of film |

depending on the applied contact pressure. It was found that films of saliva took a considerably shorter time to thin because of their lower viscosity. Double layer repulsion may be a feature common to many other biological lubricants.

## Action of Synovial Fluid

The results described in this article suggest that there are short range electrical repulsive forces in synovial fluid which, by preventing solid contact between deformable surfaces, reduce wear. A thin unbroken film of fluid can thus be maintained between surfaces. The separating film for healthy fluid is about 100 Å thick when the contact pressure is of the order of 1 atm. The few experiments we have carried out with arthritic fluid indicate an equilibrium film only three-quarters of this thickness, but this can be increased to "normal" values by increasing the ionic concentration of sodium chloride. It is not possible on the basis of these limited experiments to say more than this, and it should be remembered that little is known about the intrinsic lubricating properties of such defective fluids; no experiments, as far as we know, have been carried out on healthy joints (human or animal) in which the healthy synovial fluid is replaced by arthritic fluid.

In the joint, lubrication is complicated by factors such as the interaction of the cartilage, the synovial fluid, the geometry of the joint, the speed of joint movement and the relative roles of rolling and sliding in joint motion. Recent studies have shown that synovial fluid is non-Newtonian<sup>18-20</sup>, that it can form protective gel films on cartilage<sup>21</sup>, that cartilage itself is porous<sup>22,23</sup> and may be able to "weep" reserves of liquid into the contact at points of high stress<sup>22</sup> and that cartilage is elastic<sup>22</sup> but rather rough<sup>24</sup> so that it traps pools of liquid that lead to long squeeze times<sup>24</sup>. From these properties, the concept of boosted lubrication by fluid entrapment and gel film enrichment has been formulated<sup>25-27</sup>. The properties are of great

mechanical advantage to the joint and presumably provide something special for each regime of lubrication. Only when cartilage surfaces approach closely may the benefits of double layer repulsion be felt. It provides an "electrical cushion" that may well prevent the extrusion by pressure alone of very thin boundary layers of fluid from between the surfaces.

In spite of the provisional nature of this work the results suggest that in studying the biomechanical action of living joints it is not sufficient to treat the synovial fluid solely as a liquid with unusual rheological properties. Its electrical double layer properties must also be taken into account.

I thank Dr D. Tabor for advice and encouragement, Dr A. A. Watson for samples of synovial fluid and for identifying the joint conditions, Dr J. Lines for biochemical advice and Professor D. Dowson and his colleagues for discussions of recent work and general advice. The work was supported by the Science Research Council and E. I. du Pont de Nemours Co. The rubber surfaces were prepared by the Avon Rubber Company Ltd.

Received November 16, 1970; revised January 25, 1971.

- Roberts, A. D., and Tabor, D., *Nature*, **219**, 1122 (1968).
- Roberts, A. D., and Tabor, D., *Disc. Faraday Soc.* (in the press).
- Roberts, A. D., *Eng. Materials Design*, **11**, 579 (1968).
- Wright, V. (ed.), *Lubrication and Wear in Joints* (Sector, London, 1969).
- Charnley, J., *Proc. Symp. Biomechanics*, London (Inst. Mech. Eng., 1959).
- Ropes, M. W., Robertson, W., Rossmeisl, E. C., Peabody, B., and Bauer, W., *Acta Med. Scand. Suppl.*, **196**, 700 (1947).
- Roberts, A. D., *Brit. J. Appl. Phys.*, **4**, 423 (1971).
- Ogston, A. G., and Stanier, J. E., *J. Physiol.*, **119**, 244 (1953).
- Mysels, K. J., and Jones, M. N., *Disc. Faraday Soc.*, **42**, 42 (1966).
- Barclay, L. M., and Ottewill, R. H., *Disc. Faraday Soc.* (in the press).
- Balazs, E. A., *Fed. Proc.*, **17**, 1086 (1958).
- Preston, B. N., Davies, M., and Ogston, A. G., *Biochem. J.*, **96**, 449 (1965).
- Laurent, T. C., *Fed. Proc.*, **25**, 1037 (1966).
- Radin, E. L., Swann, D. A., and Weissner, P. A., *Nature*, **228**, 377 (1970).
- Reynolds, O., *Trans. Roy. Soc.*, **177**, 157 (1886).
- Bauer, W., Ropes, M. W., and Waine, H., *Physiol. Rev.*, **20**, 272 (1940).
- Davies, D. V., *Proc. Inst. Mech. Eng.*, **181**, part 3J, 25 (1967).
- Ogston, A. G., and Stanier, J. E., *Biochem. J.*, **46**, 364 (1950).
- Negami, S., thesis, Univ. Lehigh, Bethlehem, Pennsylvania (1964).
- Davies, D. V., and Palfrey, A. J., *Fed. Proc.*, **25**, 3 (1966).
- Maroudas, A., *Proc. Inst. Mech. Eng.*, **181**, part 3J, 122 (1967).
- McCutchen, C. W., *Nature*, **184**, 1284 (1959).
- Edwards, J., *Proc. Inst. Mech. Eng.*, **181**, part 3J, 6 (1967).
- Dowson, D., Longfield, M. D., Walker, P. S., and Wright, V., *Proc. Inst. Mech. Eng.*, **182**, part 3N, 68 (1968).
- Walker, P. S., Dowson, D., Longfield, M. D., and Wright, V., *Ann. Rheum. Dis.*, **27**, 512 (1968).
- Walker, P. S., Sikorski, J., Dowson, D., Longfield, M. D., and Wright, V., *Ann. Rheum. Dis.*, **28**, 1 (1969).
- Longfield, M. D., Dowson, D., Walker, P. S., and Wright, V., *Bio-Med. Eng.*, **4**, 517 (1969).
- Wright, V., Haslock, D. I., Dowson, D., Sellar, P., and Reeves, B., *The Evaluation of Silicone as an Artificial Lubricant in Osteoarthrotic Joints* (in the press).

**Table 2** Viscosity Data for Synovial Fluid Specimens

| Viscosity method              | Squeeze |       |       | Instantaneous tangential shear |        |        |
|-------------------------------|---------|-------|-------|--------------------------------|--------|--------|
| Shear rate (s <sup>-1</sup> ) | 75      | 50    | 25    | 10,000                         | 16,000 | 22,000 |
| Film thickness (Å)            | 10,000  | 5,000 | 1,000 | 500                            | 300    | 200    |
| Specimen viscosities (cP)     |         |       |       |                                |        |        |
| A                             | 40      | 60    | 100   | 200                            | 260    | 390    |
| B                             | 140     | 400   | 450   | —                              | —      | —      |
| C                             | 180     | 320   | 380   | 170                            | 200    | 310    |
| D                             | 90      | 110   | 180   | 200                            | 300    | 400    |
| E                             | 70      | 120   | 230   | 200                            | 250    | 300    |
| F                             | 90      | 100   | 190   | 130                            | 220    | 400    |

# LETTERS TO NATURE

## PHYSICAL SCIENCES

### Extragalactic X-ray Sources and Associations of Galaxies

RESULTS from sounding rocket experiments, confirmed and extended by data from the UHURU satellite, have revealed the existence of cosmic X-ray sources at high galactic latitude which apparently coincide with well known external galaxies. The first of these reported was M87 (ref. 1) followed by NGC-5128 and 3C273 (ref. 2). More recently NGC1275 (refs. 3 and 4) and NGC4151 (ref. 4) have been reported to be X-ray sources. Finally, a source has been reported in the direction of the Coma Cluster which has not yet been associated with a single galaxy (paper presented by H. G., E. M. Kellogg, C. Leong, H. Tananbaum and R. Giacconi at Amer. Phys. Soc. Meeting, March/April 1971). The results from UHURU on these and other subjects are listed in Table 1.

**Table 1** Extragalactic Objects observed by UHURU

| Name              | Distance (Mpc) | 2.6-6.9 keV X-ray flux (ergs/cm <sup>2</sup> s) | 2.6-6.9 keV X-ray luminosity (erg/s) |
|-------------------|----------------|-------------------------------------------------|--------------------------------------|
| 3C273             | 630            | $7 \times 10^{-11}$                             | $3 \times 10^{45}$                   |
| Coma (?)          | 90             | $1 \times 10^{-10}$                             | $1 \times 10^{44}$                   |
| Perseus (NGC1275) | 70             | $4 \times 10^{-10}$                             | $2 \times 10^{44}$                   |
| Virgo (M87)       | 15             | $2 \times 10^{-10}$                             | $5 \times 10^{42}$                   |
| NGC4151           | 13             | $5 \times 10^{-11}$                             | $1 \times 10^{42}$                   |
| NGC5128           | 5              | $8 \times 10^{-11}$                             | $3 \times 10^{41}$                   |
| SMC               | 0.054          | $2 \times 10^{-10}$                             | $6 \times 10^{37}$                   |
| LMC               | 0.052          | $7 \times 10^{-10}$                             | $2 \times 10^{38}$                   |

M87 has been suggested to be time variable<sup>5,6</sup>. There is a published<sup>4</sup> upper limit of  $3 \times 10^{42}$  erg/s on NGC1068. Also, M82 should emit less than  $10^{41}$  erg/s and M31 less than  $5 \times 10^{39}$  erg/s (private communication by E. Kellogg, C. Leong and S. Murray).

We wish to draw attention to some patterns of the data as they stand now, and point out some evidence for a class of intense X-ray sources correlated with associations of galaxies. The accompanying phenomena, and thus possibly the X-ray emission, extend well beyond the confines of one galaxy. The evidence for this view is, first, that the data from the direction of M87 show that more than a single source is involved; a region about  $1^\circ$  in size and containing M87 is found to be emitting X-rays<sup>7</sup>. Furthermore, the source in Coma, the one near NGC1275 and the one near M87 (the three brightest sources after 3C273), lie in regions where peculiar associations of galaxies are also found (compare refs. 8-11). These associations are rich in E and SO galaxies and show structures in optical and radio.

Particularly noteworthy are the sources in Perseus and Coma, for which the X-ray luminosities are in excess of  $10^{44}$  erg/s. In both of these areas it has been suggested from radio observations<sup>10,11</sup> that a centre of activity would blow an (anisotropic) galactic wind onto nearby bodies. In Perseus the involved galaxies are NGC1275 (the centre of activity suggested in ref. 10), NGC1265 and IC310; this region of the Perseus Cluster also contains two lines of galaxies<sup>8</sup>. In Coma, the involved galaxies are thought to be NGC4874 (the centre of a past and weaker activity suggested in ref. 11) and NGC4869.

In both cases extensive ( $\approx 26'$  and  $40'$ ) haloes have been observed at 408 MHz.

In Virgo the source with an X-ray luminosity  $\approx 5 \times 10^{42}$  erg/s is close to M87 which shows internal compact and jetlike structures; a line of E galaxies goes through M87 in the same direction as the jet<sup>8</sup>. Finally, it has been indicated<sup>8</sup> that the radio galaxy NGC5128, which has an X-ray luminosity  $\approx 3 \times 10^{41}$  erg/s, is the centroid of a loose (or dispersing) chain of galaxies.

It will be noted that the regions of the three brightest sources are further imbedded in very dense areas; in fact, they are close to the centroids of the Coma Cluster, of the so called Perseus Cluster, and of the Virgo Cluster proper. It is open to question, as we briefly discuss below, whether the correlation with dense areas—compact clusters or subcondensations—is trivial or intrinsic to the physical nature of the sources.

In any case, the above considerations lead naturally to a grouping of these three sources into a class III with an X-ray luminosity ranging from some  $10^{44}$  erg/s to some  $10^{42}$  erg/s. But then, other galaxies in Table 1, such as NGC4151, other conventional Seyferts and M82 which are active, but not imbedded in a peculiar environment, are conveniently grouped into another class II, which by now happens to range from  $10^{42}$  to perhaps  $10^{40}$  erg/s; NGC5128 is ambiguous. The normal galaxies such as the Magellanic Clouds, the Milky Way and M31 fall into a class I which extends below  $10^{40}$  erg/s.

If indeed it will emerge that a reasonably well defined, empirical class of X-ray sources is correlated with associations of galaxies, there are still several possibilities concerning their physical natures which call for specific observations. First, the dominant X-ray emission is localized. An extreme point of view would be that the main emission is from an unseen centre of activity<sup>8</sup> from which the association of galaxies originated. This would obviously imply a persistent lack of identification with a conspicuous galaxy. Rather, the main source should peak near the centroid of the association of galaxies.

If the emission is localized on a galaxy, this will indicate that one active nucleus is responsible for the peculiar appearance of the whole surrounding group. A compact, nonthermal, highly variable, nuclear source is to be expected, in agreement with the notion that large quantities ( $10^{43}$ – $10^{46}$  erg/s) of relativistic particles must flow out of the galaxy. NGC1275 is the obvious candidate in Perseus. In Coma, NGC4874 would be the first candidate as it seems to be the likely centre for the activity in radio. In this case, however, the X-ray power of NGC4874 would exceed that corresponding to the presently observed radio structures, as given in ref. 11; only a flat nonthermal spectrum extrapolated back from the X-ray to lower frequencies would be consistent with an absence of nonthermal optical and infrared emission. On the other hand, there are several objects at the centre of the Coma Cluster (not all definitely members) which show jets and peculiar structures<sup>12</sup>, the other conventional indicators of violent activity.

Second, the emission may be due to a superposition of individual galaxies comprising the associations, each with an X-ray luminosity  $L_x \approx 10^{42}$ – $10^{43}$  erg/s. In this case one would expect at low resolutions an extended size, in the case of Virgo up to two degrees with few emitters. Finally, the emission



from intracluster gas heated either by explosive activity in the region or by the motions of the galaxies<sup>13,14</sup> can be dominant. The X-ray source in this case should be extended and have a thermal (though likely not isothermal) spectrum. This possibility appears to be excluded for the Virgo Cluster, where time variability has been reported; but it is more likely for a rich and compact system as the Coma Cluster.

We acknowledge discussions with the UHURU Group, especially with E. Kellogg, C. Leong and S. Murray. We thank also G. Burbidge, P. Morrison, M. Rees and G. Spada for helpful discussions. This research was supported by NASA.

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- <sup>1</sup> Byram, E. T., Chubb, T. A., and Friedman, H., *Science*, **152**, 66 (1966).
- <sup>2</sup> Bowyer, C. S., Lampton, M., Mack, J., and de Mendonca, F., *Astrophys. J. Lett.*, **161**, L1 (1970).
- <sup>3</sup> Fritz, G., Davidsen, A., Meekins, J. F., and Friedman, H., *Astrophys. J. Lett.*, **164**, L81 (1971).
- <sup>4</sup> Gursky, H., Kellogg, E. M., Leong, C., Tananbaum, H., and Giacconi, R., *Astrophys. J. Lett.*, **165**, L43 (1971).
- <sup>5</sup> Byram, E. T., Chubb, T. A., and Friedman, H., *Nature*, **229**, 544 (1971).
- <sup>6</sup> Janes, A. F., Pounds, K. A., Ricketts, M. J., and Rees, M. J., *Nature*, **230**, 188 (1971).
- <sup>7</sup> Kellogg, E., Gursky, H., Leong, C., Schreier, E., Tananbaum, H., and Giacconi, R., *Astrophys. J. Lett.*, **165**, L49 (1971).
- <sup>8</sup> Arp, H., *Pub. ASP*, **80**, 129 (1968).
- <sup>9</sup> Burbidge, G., and Burbidge, E., *Nature*, **224**, 21 (1969).
- <sup>10</sup> Ryle, M., and Windram, M. D., *Mon. Not. Roy. Astron. Soc.*, **138**, 1 (1968).
- <sup>11</sup> Willson, M. A. G., *Mon. Not. Roy. Astron. Soc.*, **151**, 1 (1970).
- <sup>12</sup> Rood, H. J., *Pub. ASP*, **80**, 424 (1968).
- <sup>13</sup> Felten, J. I., Gould, R. J., Stein, W. A., and Woolf, N. J., *Astrophys. J.*, **146**, 955 (1966).
- <sup>14</sup> Ruderman, M. A., and Spiegel, E. A., *Astrophys. J.*, **165**, 1 (1971).

## Ionospheric Undulations following Apollo 14 Launching

Chimonas and Hines<sup>1</sup> predicted that a supersonic shock within the atmosphere would be followed by ionospheric disturbances observable from some distance. Such effects were observed during the total solar eclipse of March 7, 1970 (ref. 2). Similar ionospheric effects are to be expected when a large missile and its exhaust plume travel with supersonic velocity close to ionospheric heights. This effect was observed at Fort Monmouth, New Jersey, on January 31, 1971, after the Apollo 14 launching. Ionograms taken from vertical sounding at the Red Hill Station (74° 07' 52" W long.; 40° 23' 25" N lat.)

every 5 min have been converted to true-height electron-density profiles (Fig. 1). Each curve in the figure describes the true height variation of a noted plasma frequency (MHz). Since sporadic-E was present during part of the experiment, the figure is restricted to F-region data. Three successive compressions or undulations within the lower part of the region are indicated. The second undulation, however, is noticeable throughout the entire bottomside region.

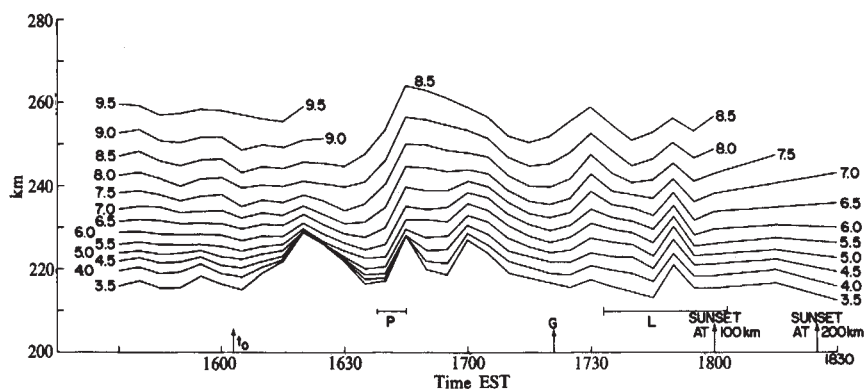
The effective velocity related to the arrival times of the maximum compression of these ionospheric deviations was estimated as follows. The lift-off time,  $\pm 0$ , is marked in the figure. Generation of the supersonic impulses occurs some time after lift-off, that is, about  $\pm 0 + 2$  min. The noted three signals arrive 15, 40 and 55 min later. The great-circle distance from the launching site to our station is about 1,440 km. The front of the produced wake can be assumed to be approximately west-to-east. Assuming a single wake front travelling northward, we can estimate, from the geometry of the locations, the travel distance of this front. A reasonable value is 1,275 km. From this distance, we find for the three disturbances the effective group velocities of about 1.42, 0.53 and 0.39 km s<sup>-1</sup> respectively.

Some facts are of particular interest. The build-up time for the first ionospheric compression is rather long; about twice as long as that observed for the second and third deviations. Further, the second impulse was observed throughout the bottomside F-region, in addition to a compression at lower altitudes. The F-region was pushed upward by about 20 km during the second pulse whereas only the compression was seen with the other deviations. This compression, however, was less pronounced for the third pulse.

To interpret the observed signal sequence, we follow the explanation given by Wickersham<sup>3</sup> for vertical ionospheric disturbances generated by nuclear explosions. These disturbances have been previously reported by Daniels *et al.*<sup>4</sup>. Wickersham ascribed the two signals observed after nuclear explosions to an ion acoustic mode and a normal acoustic mode. A sound wave propagating upward will, on reaching an altitude of about 160 km, become separated into an ion acoustic wave and a neutral acoustic wave. The former will travel fast with supersonic speed. For this fast component, Wickersham calculated a velocity at 250 km altitude of 1.37 km s<sup>-1</sup> which is close to our observation of 1.42 km s<sup>-1</sup> for the first signal and close to the value of 1.28 km s<sup>-1</sup> deduced from nuclear explosions. The supersonic component will be substantially damped at altitudes above 250 km for group velocities close to 1 Hz. Higher frequency signal components will be attenuated even stronger. This explains the observed slow build-up time of the first signal and its restriction to altitudes below 250 km (see Fig. 1).

Our value of 0.53 km s<sup>-1</sup> for the group velocity of the second signal is close to the 200 km altitude value of 0.526 km s<sup>-1</sup> deduced from nuclear explosions. Both values, however, are somewhat low in comparison with the speed of sound in a neutral medium as calculated by Wickersham for a standard

**Fig. 1** True height variation for plasma frequencies indicated (MHz). The lift-off time is marked  $t_0$ . The arrival time of the acoustic signal on the ground is marked G. The intervals marked P and L indicate times during which acoustic precursor (P) or late-coming (L) signals have been observed for lift-off of other missiles. Corresponding acoustic measurements were not possible because of strong winds at Fort Monmouth during the ascent of Apollo 14. The general trend of the bottomside ionosphere reflected in the figure is dictated by local time which is approaching sunset as indicated.



atmosphere. Both values correspond to an altitude of about 130 km in that calculation. But any reference to a standard atmosphere may suffer from uncertainties regarding the assumed parameters, for example, temperature. Thus, we agree with Wickersham that the observed velocities are acceptable as acoustic speeds in a neutral medium. This statement is further supported by the fact that our second signal, the normal acoustic signal, affected all regions of the bottomside ionosphere; it was not restricted to altitudes below 250 km as was the first signal. The onset of this second signal was observed earlier at altitudes higher than 220 km. For example, the onset at 243 km occurred about 10 min earlier than at 220 km. For the onset at 243 km one finds a velocity of  $0.85 \text{ km s}^{-1}$ , which is close to Wickersham's calculation of  $0.825 \text{ km s}^{-1}$  for an altitude of 250 km.

The third signal of our observations cannot be correlated to the cited disturbances from nuclear explosions. The character of the signal suggests an ion acoustic mode because the ionospheric height deviations were not observed above 243 km. The low altitude compression from the third signal is much smaller than the compression observed from the first two signals. One can therefore assume some attenuation along the path of the third signal, for example, an indirect path produced by reflexion appears possible. On the other hand, the possibility of a second source of sound has to be considered, that is the sound from re-entry of the shell of the first stage. We calculated from time and location of the separation of the first and second stages a signal velocity of about  $0.40 \text{ km s}^{-1}$  for the identification of the re-entry signal with our third signal. The point of origin of the re-entry signal would be below 160 km altitude. Thus, the signal would for some part of its path travel in a mode coupling the ion acoustic mode with the normal acoustic mode. Only after mode separation, that is above 160 km altitude, can an ion acoustic mode develop. Under this condition, a fourth signal closely following the ion acoustic mode should have been observed. At 17.30 EST, there indeed exists a small upward motion in the entire bottomside ionosphere. But it does not seem advisable to correlate this motion with such a second normal acoustic mode because no compression was observed at low altitudes. Thus, we are left with the more plausible explanation that our third signal either followed an indirect path or was originated by the re-entry of the first stage, but was travelling in a normal acoustic mode rather than in an ion acoustic mode.

It would help if similar observations were made simultaneously at different distances from the launching site. If the concept suggested by C. O. Hines of a shock front travelling with diminishing velocity is correct, such observations would show decreasing effective group velocities for increasing distances until the normal velocity of sound would ultimately be reached.

The undulations differ from the undulation observed during the solar eclipse when the shock was effective over a wide range of altitudes. The missile shock was restricted to the trajectory and the dimensions of the exhaust plume. It is therefore not surprising that the missile launching was not recorded by simultaneously performed observations of the total ionospheric electron content. During the eclipse, the electron content measurements (performed with ATS-3 polarization measurements) showed typical undulations which were also reflected by electron density profiles derived from bottomside sounding (such as those in Fig. 1). During and after the Apollo 14 launch, the total electron content fluctuation, that is  $(\Delta f N d h / f N d h)^2$ , was always smaller than  $10^{-4}$ . No content undulations were observed. It can be assumed that phase cancellations prohibited a low altitude effect from the shock front upon the electron content integration along the path from our station toward ATS-3. A direct effect from the rocket is not to be expected. The rocket passed at about 200 km altitude underneath the radio path which at the crossing point was about 450 km higher. The ion acoustic waves could not reach the high ionospheric regions above

the rocket. The normal sound wave may have been confined within the exhaust plume of the second stage, and the density boundaries of that plume may have prevented an upward motion of any signal.

It is interesting to compare our ionospheric observations with acoustic measurements of the missile noise for the same and similar distances performed during many missile launchings<sup>5</sup>. These acoustic measurements record the direction and time of signal arrival at the ground. In addition to the signal travelling with normal velocity of sound, supersonic precursor signals (often two) and infrasonic latecoming signals are observed. Time intervals during which those supersonic and infrasonic signals were observed have been reported in the literature. These intervals are shown in Fig. 1 and are marked P and L, respectively. Measurements of this type were not possible at Fort Monmouth because of strong local winds during the Apollo 14 ascent. The expected acoustic precursor time, marked P, is rather close to the strongest ionospheric deviation observed (second deviation in Fig. 1). During the rather wide range (marked L in Fig. 1), when latecoming acoustic signals may be expected, one sees, at 17.50 EST, a small upward motion of the ionospheric region. Such small ionospheric motions, however, are often observed. In fact, a similar motion was recorded about one hour before lift-off (not shown in Fig. 1).

It is too early to discuss the possible mechanisms interlinking ionospheric undulations with the arrival of the mentioned acoustic signals. For such mechanisms one must consider the fact that the acoustic signals travel at the normal velocity of sound along the microphone arrays on the ground, independently of whether they are related to precursing, normal, or late arrival. Another fact is also noted: when acoustic precursor signals were observed at various stations at increasing distances from the launching site, the effective acoustic group velocity was found to decrease with increasing distance. A similar mechanism was stipulated above for a shockfront at ionospheric heights.

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Received May 18, 1971.

<sup>1</sup> Chimonas, G., and Hines, C. O., *J. Geophys. Res.*, **75**, 875 (1970).

<sup>2</sup> Arendt, P. R., *Nature Physical Science*, **230**, 89 (1971).

<sup>3</sup> Wickersham, A. F., in *Phase and Frequency Instabilities in Electromagnetic Wave Propagation* (edit. by Davies, K.), 421 (Technivision Services, Slough, England, No. 33 AGARD Conf. Proc., 1970).

<sup>4</sup> Daniels, F. B., Bauer, S. J., and Harris, A. K., *J. Geophys. Res.*, **65**, 1848 (1960).

<sup>5</sup> Kaschak, G. R., *J. Geophys. Res.*, **74**, 914 (1969).

## Recent Faulting near the Volta Dam

RECENT faulting on the Volta river, discussed recently by *Nature's* geomagnetism correspondent<sup>1</sup>, cannot be taken as evidence "that many of the Earth's Pre-Cambrian shield areas should now be classified as earthquake hazards" because the Volta dam does not lie in a typical shield area.

Seismicity near the Volta dam results from the Chain fracture zone which reaches Africa at Accra<sup>2</sup>. The suggestion that this fracture zone runs up the Benue trough<sup>3</sup> fails to allow for the change in South Atlantic rotation poles between the Mesozoic and the Tertiary and fails to match ridge and continental margin offsets. It is therefore geometrically impossible. The Benue trough lies over a Cretaceous rift which extended north-east from an RRR triple junction under the present site of the Niger delta. Misfit motion in the African plate closed this rift in Santonian time<sup>4</sup>.



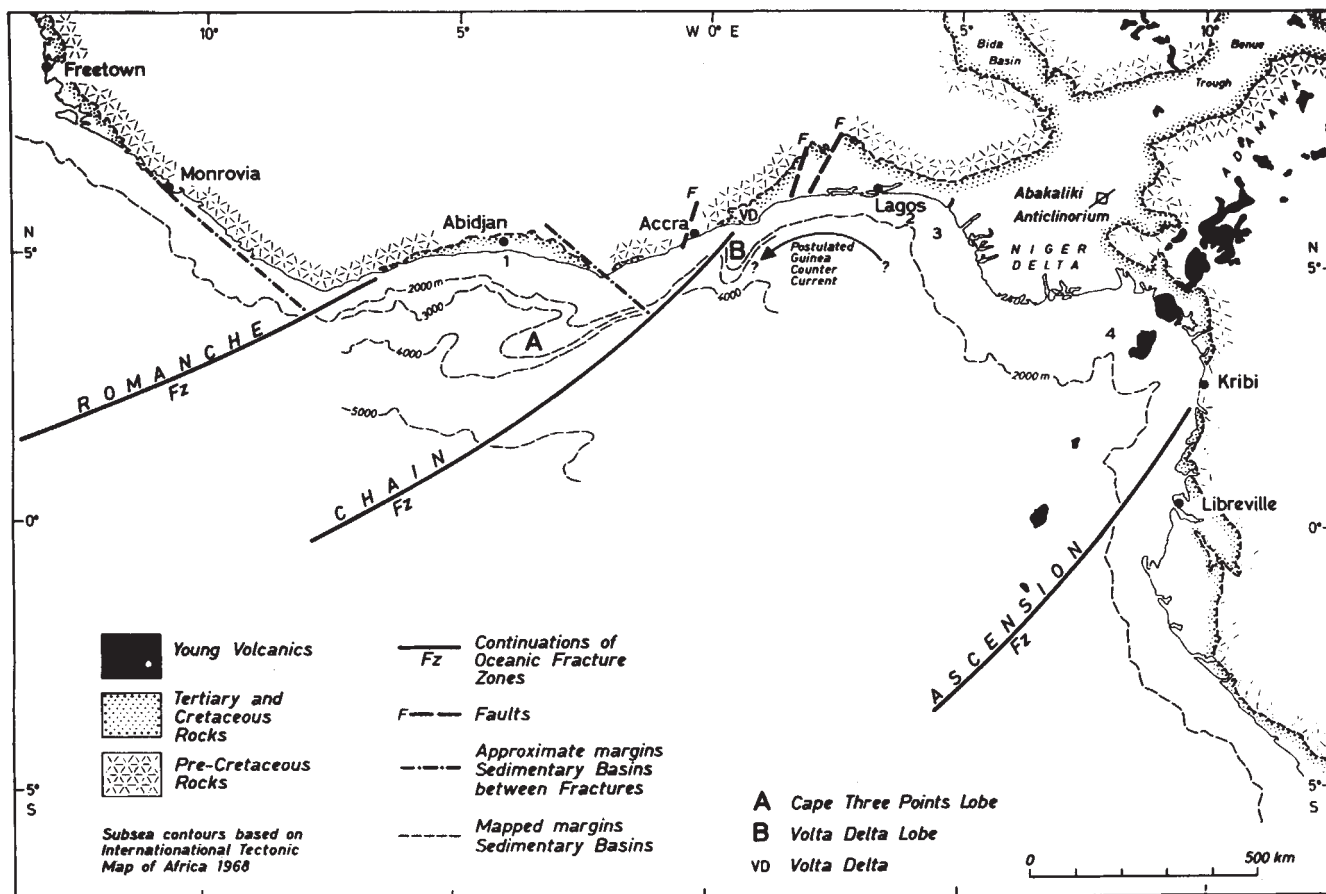


Fig. 1 Structure of the Accra seismic area. (The Volta dam lies at the letter F north of Accra.) The Gondwana continent split in early Cretaceous times along a rift close to the margins of the sedimentary basins and along transforms now marked by the fracture zones. An RRR junction lay under the present site of the Niger delta and a short lived rift extended up the Benue trough. The transform at the edge of the Ghana continental shelf has survived as a topographic feature because it has been scoured by the Guinea counter-current during the past 150 m.y. Continuing seismic activity at Accra perhaps results from the exceptionally abrupt continental/oceanic crust boundary at the shelf edge. Submarine canyons: 1, Trou Sans Fond; 2, Avon's Canyon; 3, Mahin Canyon; 4, Calabar Canyon.

Differential lateral motion across the Chain fracture zone at the continental margin is unlikely because the coast of Africa lies beyond the mid-Atlantic ridge offset. The seismicity is more probably related to an abrupt change from crust of continental thickness to crust of oceanic thickness at the edge of the Ghana continental shelf.

The transform fault forming the edge of the Ghana continental shelf developed in the early Cretaceous and its survival as a topographic feature (perhaps the world's oldest) I attribute to the geostrophic Guinea counter-current<sup>5</sup> which has scoured the fault scarp and prevented sediment accumulation throughout 150 m.y. The underwater lobe of the young Volta delta has been diverted westward by the current (Fig. 1) which has also scoured the continental slope of the Dahomey basin and deposited the Cape Three Points lobe, an analogue of the Blake-Bahama outer ridge.

Bouguer anomalies in the Accra area<sup>6,7</sup> indicate a change in crustal structure within the continent across the eastern boundary of the West African Craton<sup>8-10</sup>. This change, which resulted from the development of the Dahomey suture in an early Palaeozoic paratectonic orogeny<sup>11</sup>, localized the Cretaceous transform that split the Gondwana continent and became the Chain fracture zone.

The seismic area near Accra extending along the Akwapim fault<sup>12</sup> to the Volta dam site owes its existence to a peculiar if not unique combination of circumstances and is far from being a typical Pre-Cambrian shield area.

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- <sup>1</sup> *Nature*, **229**, 371 (1971).
- <sup>2</sup> Burke, K., *Nature*, **222**, 655 (1969).
- <sup>3</sup> Fail, J. P., Montadert, L., Delteil, J. R., Valery, P., Patriat, P., and Schlich, R., *Earth Planet. Sci. Lett.*, **7**, 413 (1970).
- <sup>4</sup> Burke, K., Dessauvage, T. F. J., and Whiteman, A. J., *Proc. Conf. African Geol.*, Ibadan (1970, in the press).
- <sup>5</sup> Martin, L., *Bull. d'ASEQUA*, **25**, 8 (1970).
- <sup>6</sup> ORSTOM, *Mesures gravimétriques et magnétique en Afrique Occidentale* (1960).
- <sup>7</sup> *Anomalies de Bouguer Europe-Africa* (Bureau Gravimétrique International, Paris, 1967).
- <sup>8</sup> Kennedy, W. Q., in *Salt Basins Around Africa* (Inst. Petrol., London, 1965).
- <sup>9</sup> Grant, N. K., *Nature*, **215**, 609 (1967).
- <sup>10</sup> Fitches, W. F., *Nature*, **226**, 744 (1970).
- <sup>11</sup> Burke, K., and Dewey, J., *J. Mining Geol. Nig. Min. Geol. Met. Soc.*, **6**, 75 (1971).
- <sup>12</sup> Burke, K., *J. Mining Geol. Nig. Min. Geol. Met. Soc.*, **4**, 29 (1969).

## Mercury in a Coastal Marine Environment

INCREASING attention has been given recently to mercury pollution, especially in rivers and lakes, and to the movement of the element in aquatic food chains (reviewed in ref. 1). Most information has been obtained for situations where the environmental concentrations have been increased through local use of fungicides containing mercury, the presence of such compounds in wastes from the wood pulp and paper industries or the discharge of other industrial wastes.

According to Klein and Goldberg<sup>2</sup> mercury enters the oceans at comparable rates as a result of both human activities and continental weathering. The oceanic residence time of

mercury is  $\sim 10^4$  yr (ref. 3) so that human activities cannot yet have had a significant influence on the amounts of the element in the marine environment considered on a wide scale, whatever the effects on restricted environments. As a basis for the assessment of the problems of mercury pollution it is essential to learn more about the distribution and behaviour of the element in environments which have been subject to low or negligible pollution. We report here some initial findings of investigations carried out in Southampton Water and the English Channel with these considerations in mind.

Mercury in natural waters was determined spectrophotometrically with dithizone, after preliminary concentration and separation. Samples of 20–40 l. were acidified to 0.1 N with sulphuric or purified hydrochloric acid and mercury 203 was added as an isotopic dilution tracer. Mercury was adsorbed as a chloro-complex on anion exchange resin and eluted in a 1:5 solution of 45% (w/w) perchloric acid and ethyl acetate. After removal of ethyl acetate, mercury was extracted as the dithizone complex from the diluted perchloric acid into chloroform, back extracted into 5 N hydrochloric acid and finally measured spectrophotometrically after a further extraction with dithizone. The concentration found was corrected for the recovery of the tracer (generally about 90%). Reagent blanks were determined on distilled water and blanks were also run on seawater stripped of mercury. The samples analysed were not filtered and the concentrations reported include that fraction of the mercury associated with the particulate matter, which was leached by the dilute acid. Separate investigations showed that this fraction was not greater than 10% of the dissolved mercury.

Mercury in organisms and sediments has been determined by neutron activation analysis of freeze-dried material. The irradiated material was digested under reflux in the presence of mercury carrier with concentrated sulphuric acid and 50% (w/v) hydrogen peroxide. The mercury was then distilled as the chloride and, after further radiochemical purification, mercury 203 was measured by counting the  $\beta$  particles. The procedures developed for waters and other materials will be described more fully elsewhere.

The concentrations found in some water samples are given in Table 1. The standard errors are based on measurements made on replicate samples collected on each occasion. The values for seawater outside Southampton Water vary between 0.014 and 0.021  $\mu\text{g/l}$ . There are few other data for mercury with which these values may be compared. Stock and Cucuel<sup>4</sup> found 0.03  $\mu\text{g/l}$  in water collected off Heligoland. Water from the area of the Ramapo Deep in the north-western Pacific has been reported<sup>5,6</sup> to contain from 0.08 to 0.27  $\mu\text{g/l}$  with the highest values occurring in deep water. It is not possible at present to suggest the extent to which these differences reflect genuine regional variations rather than analytical effects. It seems probable that the higher values of 1.6 to 3.6  $\mu\text{g}$  total Hg/l. found<sup>7</sup> for oxidized samples of water from Minamata Bay, Japan, were related to the serious

contamination of that region<sup>8</sup> but comparisons are again complicated by uncertainties as to the forms of mercury measured by different procedures.

River water entering Southampton Water in the Rivers Test and Itchen contained 0.010  $\mu\text{g/l}$ , considerably less than the annual mean concentration of 0.066  $\mu\text{g}$  of dissolved Hg/l. reported for the Saale<sup>9</sup>. The concentration in river water was thus somewhat lower than that in the estuary and the open water of the English Channel.

Mercury was determined in five specimens of the mollusc *Mercenaria mercenaria* from various parts of Southampton Water, where it is abundant. The concentrations in whole organisms, without shell, ranged from 0.18 to 0.57 p.p.m. dry weight (0.03 to 0.12 p.p.m. wet weight). Values reported<sup>2,10</sup> for various molluscs, including *Mercenaria*, collected off the coasts of North America are in the higher but overlapping range of 0.4 to 21 p.p.m. dry weight.

Do the concentrations in *Mercenaria* from Southampton Water reflect anything other than natural environmental processes? Our results show that the amounts of mercury in the river and estuarine waters are low. Three samples from the surface of the bottom mud in different parts of the estuary had mercury contents ranging from 0.19 to 0.64 p.p.m. Two samples of mud from underlying anoxic layers, at depths of about 10 cm, contained 2.2 and 5.7 p.p.m., showing that pronounced enhancement can occur in reducing conditions. The former values are within the range of 0.02 to 1 p.p.m. reported by Klein and Goldberg<sup>2</sup> for surface sediments off the Californian coast. They considered that their higher values may have been influenced by sewer discharges. We know no significant local sources of mercury-containing industrial wastes but have as yet no evidence on the concentration of the element in sewage effluents. The role of sediments in the transport of mercury in food chains could clearly be significant, particularly for bottom living, suspension feeding animals and may be particularly important in estuaries where considerable resuspension of sediment can occur.

Various recommendations have been made regarding "practical residue limits" for mercury in foods<sup>1,11,12</sup>. For fish eaten by man a temporary limit of 1 p.p.m. fresh weight was set in Sweden in 1967 while a limit of 0.5 p.p.m. is applied in North America<sup>13</sup>. The average concentration of total mercury (0.44 p.p.m. dry weight or 0.08 p.p.m. fresh weight) in the tissues of *Mercenaria* from Southampton Water is about one order of magnitude lower than these limits and we do not know that a major fraction of this mercury is present in the form of the more hazardous methylmercury as is generally the case for fish<sup>14</sup>. Nevertheless the attainment of these levels in shellfish in an environment which is not known to be affected by any significant mercury pollution emphasizes the need for clarification not only of natural background concentrations but also their relation to the permissible limits for sea foods.

This work was supported by the Natural Environment Research Council. T. M. L. thanks the council for a research studentship.

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Received March 22, 1971.

- Ackefors, H., Löfroth, G., and Rosén, C.-G., *Oceanogr. Mar. Biol. Ann. Rev.*, **8**, 203 (1970).
- Klein, D. H., and Goldberg, E. D., *Envir. Sci. Technol.*, **4**, 765 (1970).
- Goldberg, E. D., in *Chemical Oceanography* (edit. by Riley, J. P., and Skirrow, G.), **1**, 163 (Academic Press, London, 1965).
- Stock, A., and Cucuel, F., *Naturwissenschaften*, **22**, 390 (1934).
- Hamaguchi, H., Kuroda, R., and Hosohara, K., *J. Chem. Soc. Japan, Pure Chem. Sect.*, **82**, 347 (1961); *Chem. Abstr.*, **55**, 15222c (1961).
- Hosohara, K., *J. Chem. Soc. Japan, Pure Chem. Sect.*, **82**, 1107 (1961); *Chem. Abstr.*, **56**, 4535c (1962).

Table 1 Mercury in Sea and River Waters

| Origin *                                                              | Date of collection | No. of samples analysed | Mercury ( $\mu\text{g/l}$ ) |
|-----------------------------------------------------------------------|--------------------|-------------------------|-----------------------------|
| Test river water                                                      | Sept. 1970         | 3                       | $0.009 \pm 0.0006$          |
| Itchen river water                                                    | Sept. 1970         | 2                       | $0.010 \pm 0.001$           |
| Southampton Water                                                     |                    |                         |                             |
| Test arm ( $S=29.0^\circ/00$ )                                        | Jan. 1971          | 1                       | 0.011                       |
| Itchen arm ( $S=10.6^\circ/00$ )                                      | Jan. 1971          | 1                       | 0.010                       |
| Off Netley                                                            | Jan. 1971          | 2                       | $0.013 \pm 0.001$           |
| Solent                                                                |                    |                         |                             |
| Off Calshot ( $S=33.8^\circ/00$ )                                     | June 1970          | 6                       | $0.014 \pm 0.0008$          |
| English Channel                                                       |                    |                         |                             |
| $0^\circ 57' \text{ W } 50^\circ 40' \text{ N}$                       | July 1970          | 8                       | $0.021 \pm 0.0007$          |
| $1^\circ 00' \text{ W } 50^\circ 30' \text{ N}$ ( $S=34.7^\circ/00$ ) | Dec. 1970          | 6                       | $0.015 \pm 0.0004$          |

\* All samples were of surface water.



- <sup>7</sup> Hosohara, K., Kozuma, H., Kawasaki, K., and Tsuruta, T., *J. Chem. Soc. Japan, Pure Chem. Sect.*, **82**, 1479 (1961); *Chem. Abstr.*, **56**, 5766g (1962).
- <sup>8</sup> Kurland, L. T., Faro, S. N., and Siedler, H., *Wld. Neurol.*, **1**, 370 (1960).
- <sup>9</sup> Heide, F., Lerz, H., and Bohm, G., *Naturwissenschaften*, **44**, 441 (1957).
- <sup>10</sup> Craig, S., *J. Amer. Osteop. Assoc.*, **66**, 1000 (1967).
- <sup>11</sup> Berglund, F., and Berlin, M., in *Chemical Fallout* (edit. by Miller, H. W., and Berg, G. G.), 423 (Charles C. Thomas, Springfield, 1969).
- <sup>12</sup> Smart, N. A., *Residue Rev.*, **23**, 1 (1968).
- <sup>13</sup> *Envir. Sci. Technol.*, **4**, 890 (1970).
- <sup>14</sup> Westöo, G., in *Chemical Fallout* (edit. by Miller, H. W., and Berg, G. G.), 75 (Charles C. Thomas, Springfield, 1969).

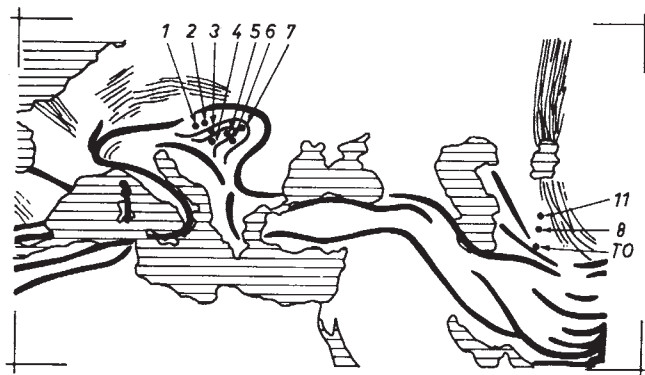


Fig. 1 Alpine and Palaeozoic orogeny (after Staub and Stille; for Hungary after Dank and Bodzay). Numbered points present the places of MTS measurements.

## Spreading Tectonics investigated by Magnetotelluric Anisotropy

MAGNETOTELLURIC anisotropy may provide an effective tool in the search for deep (0–700 km) linear structures (mid-ocean ridge, transform fault, under-thrusting) connected with ocean floor spreading.

According to the theory of magnetotelluric sounding<sup>1</sup> (MTS) in the case of horizontally stratified homogeneous layers the measured apparent resistivity versus period ( $\rho(T)$ ) are identical in all directions. In areas of geological platform and Pre-Cambrian shields, the curves of apparent resistivity  $\rho_x(T)$  referring to the direction N–S and those of  $\rho_y(T)$  referring to the direction E–W are identical or very similar. This applies to the MTS curves measured on the inner parts of the Russian platform and the Canadian shield<sup>2,3</sup>.

If these conditions of horizontal stratification are not fulfilled, the connexion between the electrical and magnetic field is given by the equation

$$E = \{Z\}H$$

where  $\{Z\}$  is the tensor of impedance. The curves of apparent resistivity  $\rho_x = 0.2T(E_x/H_y)^2$  and  $\rho_y = 0.2T(E_y/H_x)^2$  will differ from each other at a rate depending on the distortion caused by geological structure. In this way the phenomenon of "magnetotelluric anisotropy" may appear. The observed anisotropy is the greatest if the measurements are taken along the strike and dip of the geological structure. The structure which gives rise to the anisotropy may have a local or regional character. Long linear structures connected with the ocean floor spreading are regional features. To obtain definite conclusions concerning the regional structure many sounding points are needed from a large area.

The mean events of spreading tectonics take place on the accreting plate margins (mid-ocean ridges, probably the African

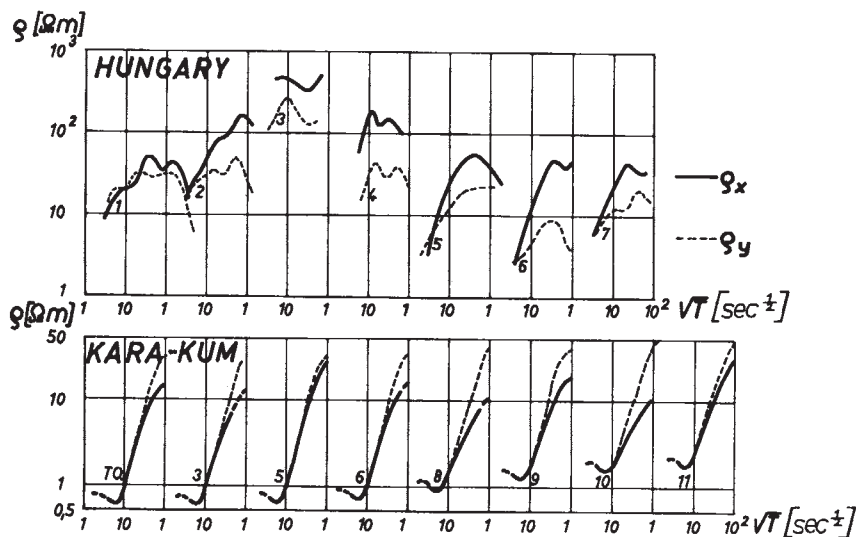
rift system, Baikal Sea and so on) and on the consuming plate margins (such as the coasts of the Pacific and Tethyan oceans)<sup>4–6</sup>. The consuming margins attributable to under-thrusting are the areas of orogenism<sup>7,8</sup>.

So far two areas are known on the consuming plate margins where MTS measurements fulfil the above conditions: the Hungarian basin and the Kara-Kum platform in the vicinity of Kopet Dag mountain (Fig. 1).

The Hungarian MTS curves (Fig. 2) show significant regional anisotropy, presumably originating from greater depth. Generally at  $T > 60$  s  $\rho_x > \rho_y$  and with increasing periods the larger axis of the anisotropy ellipse turns gradually to the N–S direction. This can be explained by two effects—the electrical anisotropy of the rocks formed by mechanical stress, and the deep regional linear structure<sup>9,10</sup>. The direction of the smaller rock-resistivity of the MTS curves and the strike of regional structure both point close to E–W. The Hungarian basin is an integral part of Alpine orogenism. The E–W directed thrusting lines in Cretaceous–Palaeogene basement have recently been detected in this area (Dank and Bodzay, personal communication). The Alpine orogeny, according to Le Pichon<sup>5</sup>, Dewey and Bird<sup>7</sup>, Dewey and Horsfield<sup>8</sup> and McKenzie<sup>11</sup>, is the result of the consummation of African and Eurasian plates, with underthrustings directed near to N–S.

The Kopet Dag mountain also belongs to the Alpine system with underthrustings, established by McKenzie<sup>11</sup>, and with great normal faults extending up to the surface. The MTS measurements were made on the platform area of the Kara-Kum desert, close to the foredeep of the Kopet Dag mountain<sup>12</sup>. All the MTS curves show regional magneto-

Fig. 2 Magnetotelluric anisotropy produced by linear structures, which developed in the course of the Alpine orogeny.



telluric anisotropy (Fig. 2) according to the linear structure. The anisotropy ellipses were not published; therefore there are no available data on the direction of their axes.

The MTS curves measured in Kamchatka<sup>13</sup> and Gruzija<sup>14</sup> also exhibit considerable anisotropy. These areas lie in the underthrusting zones of the West Pacific and Alpine system, respectively. In these areas only one pair of curves is known, therefore the connexion of the magnetotelluric anisotropy with the underthrusting of the lithospheric plate cannot be considered as proved.

We conclude that magnetotelluric anisotropy would be an effective tool in demonstrating both recent and early spreading tectonics. To exploit it, further measurements on the plate margins are necessary.

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- <sup>1</sup> Cagniard, L., *Geophysics*, **18**, 605 (1953).
- <sup>2</sup> Yanovsky, B. M., Koftun, A. A., Raspopov, O. M., and Chicherina, N. D., *Vop. Geofiz.*, **16**, 3 (1966).
- <sup>3</sup> Vozoff, K., and Ellis, R., *Geophysics*, **31**, 1153 (1966).
- <sup>4</sup> Morgan, W. J., *J. Geophys. Res.*, **73**, 1959 (1968).
- <sup>5</sup> Le Pichon, X., *J. Geophys. Res.*, **73**, 3661 (1968).
- <sup>6</sup> Isacks, B., Oliver, J., and Sykes, L. R., *J. Geophys. Res.*, **73**, 5855 (1968).
- <sup>7</sup> Dewey, J. F., and Bird, J. M., *J. Geophys. Res.*, **75**, 2625 (1970).
- <sup>8</sup> Dewey, J. F., and Horsfield, B., *Nature*, **225**, 521 (1970).
- <sup>9</sup> Ádám, A., *Acta Geodet. Geophys. Montanist.*, **4**, 187 (1969).
- <sup>10</sup> Ádám, A., *Bull. Geodet. Geophys. Res. Lab. Sopron*, **77** (1970).
- <sup>11</sup> McKenzie, D. P., *Nature*, **226**, 239 (1970).
- <sup>12</sup> Avagimov, A. A., Dubrovsky, V. G., Lagutinskaya, L. P., Nikolayeva, L. S., Solohov, V. V., Feinberg, E. B., and Sihanovic, E. L., *Res. Intern. Geophys. Res. Projects*, **4**, 182 (Nauka, Moscow, 1969).
- <sup>13</sup> Kopytenko, Y. A., Gorskov, E. S., Gorskova, I. A., Feldman, I. S., and Feldman, T. A., *Fizika Zemli*, **9**, 66 (1967).
- <sup>14</sup> Kebuladze, V. V., and Gugunava, G. E., *Fizika Zemli*, **9**, 91 (1970).

## Micro-probe Analysis and the Study of Greek Gold-Silver-Copper Alloys

Two basically gold-silver alloys<sup>1</sup> were known to the Greeks and Romans: (1) "white gold"<sup>2</sup>—a haphazard mixture derived from grains of weathered auriferous ore<sup>3</sup>; and (2) "electrum"<sup>4</sup>—an alloy of controlled quality.

A fragment of a unique Greek inscription<sup>5</sup> (late fifth century BC) records a monetary union between the cities of Mytilene and Phokaia<sup>6</sup>, which issued, jointly, a series of electrum hektai ("sixths" of a stater): unfortunately, there is no evidence for the composition of the alloy independent of that provided by the coins themselves. Chemical and spectrographic analyses<sup>7</sup> confirm that electrum contained copper (sometimes as much as 12%) and was, in practice, a ternary alloy (unpublished results of P. Meyers). The proportions of Au to Ag cannot therefore be directly determined from specific gravity measurements<sup>8</sup>. Large scale destructive analysis of valuable objects of this sort is undesirable, but improved neutron activation<sup>9</sup> and micro-probe techniques provide acceptable methods of qualitative and quantitative analysis.

This report describes the investigation of the physical properties and method of manufacture of a typical Mytilenean hekte of the fourth century BC<sup>10</sup>. The specimen is shown in Figs. 1 and 2.



Figs. 1 and 2. Obverse and reverse of Greek coin showing areas selected for micro-probe analysis. On the obverse is the head of Apollo, laureate; on the reverse is the head of a goddess (Artemis?). The weight is 2.5564 g; diameter, 10.0 mm; specific gravity, 12.46.

The experimental details and results are as follows.

(a) X-ray diffraction<sup>11</sup>: analysis showed a face-centred cubic structure with considerable line broadening consistent with local composition gradients. No evidence of ordering was observed.

(b) Radiography: radiographs obtained with a caesium source revealed no porosity<sup>12</sup>; peripheral cracks were generally visible to the naked eye.

(c) Hardness: determinations on the obverse, reverse and periphery, with a load of 25 g, showed micro-hardness varying from 247–274 HV (unprepared surface) and 188–243 HV (polished flat).

(d) Fluorescent analysis<sup>13</sup>: each side of the coin was bathed in X-rays from a tungsten target with a 50 kV excitation voltage (approximate penetration 0.5 mm): secondary X-rays emitted suggested the following average composition, by weight, for this volume of the coin: Au, 57%; Ag, 37.6%; and Cu, 5.4%. The gold content, however, was higher than that expected from the hardness and specific gravity measurements and indicated surface enrichment<sup>14</sup>. No other elements were detected by fluorescent analysis, which would have shown up all those with an atomic number higher than 22 present in concentrations of 0.15% by weight and above.

(e) Micro-probe analysis<sup>15</sup>: areas of the coin surface, both unprepared and polished, were analysed.

(i) Unprepared surface: images produced by back scattered electrons showed severe coring. The dendritic structure was most clearly seen around the outer perimeter of the coin where the surface had not been deformed by direct contact with the dies. Fig. 3 illustrates the combined effects of composition and topography. The light areas represent the gold-rich primary crystals which separate first from the melt and the darker areas between these crystals represent the metal, deficient in gold, which solidifies last. These compositional effects can be cancelled out by a suitable arrangement of the electron



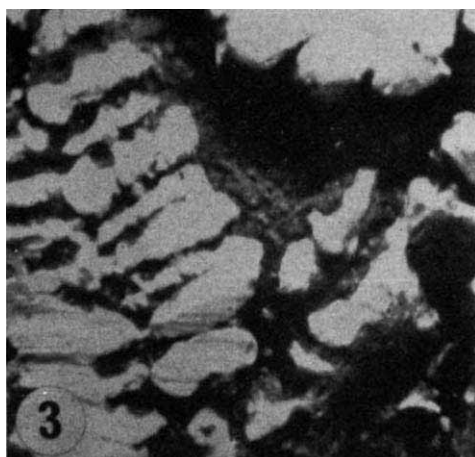


Fig. 3 Back scattered electron image from periphery of coin showing primary gold-rich dendrite ( $\times 180$ ).

counting devices, as in Fig. 4: the gold-rich areas are slightly in relief.

The figures in Table 1 are consistent with the solidification pattern suggested by Fig. 3, the centre of the dendrites being most rich in gold. The gold content decreases towards the outer edge of these primary growth crystals.

Sulphur was consistently detected towards the centre of these dendritic crystals at concentrations of 0.15–0.18% and zinc, occasionally, at the centre of some large dendrites around the head of Apollo (obverse) at concentrations of approximately 0.01%. Around the periphery of the coin the zinc content varied from 0.03–0.07%.

The figures in Table 2 were obtained from the primary dendrites which, standing slightly in relief, presented a fairly clean metallic surface. This was necessary because of the low penetration (1–2  $\mu\text{m}$ ) of the electrons used to excite the characteristic X-rays.

Between these primary crystals are wide valleys (Figs. 3 and 4) which contain a layer of dirt, thick enough to prevent the electron beam from reaching the parent metal. This layer was analysed using pure metal standards. Because no correction was made for inter-atomic effects, the figures in Table 3 are approximate.

(ii) Polished flat surface: to facilitate accurate analysis, free from the effects of topography and surface enrichment, a ground, polished flat was cut on the coin edge. The average bulk composition (by weight) was: Au,  $37.5 \pm 1.8\%$ ; Ag,  $55.0 \pm 3.7\%$ ; and Cu,  $7.5 \pm 1.9\%$ .

Experimental data suggest that the hekte was struck, with a considerable amount of cold-working, from a bead of cast electrum comparable with 9 carat gold. The presence of

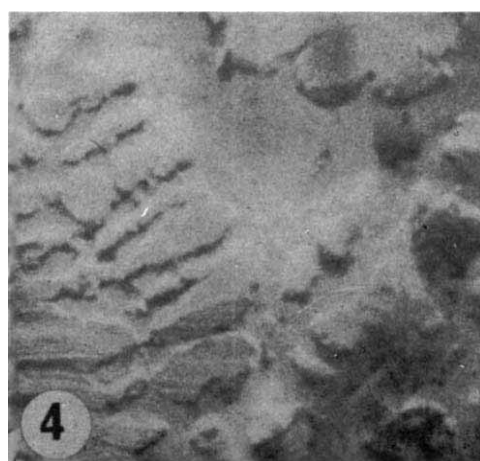


Fig. 4 Topography of field shown in Fig. 3 ( $\times 180$ ).

Table 1 Point Analyses of the Obverse Side

|                                        | Au (weight %) | Cu (weight %) | Ag (weight %) |
|----------------------------------------|---------------|---------------|---------------|
| Centre of dendrites                    | 63.5          | 6.2           | 28.4          |
|                                        | 59.2          | 12.0          | 29.3          |
| Near edge of dendrites                 | 48.3          | 11.1          | 40.1          |
|                                        | 52.6          | 6.7           | 38.8          |
|                                        | 47.1          | 6.0           | 44.9          |
| Near edge of coin, centre of dendrites | 61.5          | 8.2           | 28.8          |

Table 2 Point Analyses of the Reverse Side

|                     | Au (weight %) | Cu (weight %) | Ag (weight %) |
|---------------------|---------------|---------------|---------------|
| Centre of dendrites | 68.2          | 4.7           | 26.2          |
|                     | 62.7          | 6.8           | 29.8          |
| Edge of dendrites   | 52.3          | 9.2           | 38.1          |

Table 3 Composition

| Si    | Ca     | Al    | Mg    | Fe       | Mn               |
|-------|--------|-------|-------|----------|------------------|
| 2–18% | 20–35% | 5–15% | 6–13% | 0.1–2.5% | Small quantities |

No gold, silver or copper was detected: sulphur varied between 0.5–0.85% and zinc between 0.1–0.15%.

copper—undoubtedly a conscious addition—reflects the latitude permissible in quality control in the terms of the monetary union.

Such results, if confirmed by further experiments, would throw new light on Greek metallurgical and mint practice in the fifth and fourth centuries BC about which there is little literary evidence. They would also have repercussions on the study of hoards, particularly if any correlation is attempted between surface wear and length of circulation of electrum coins.

We thank the directors of Johnson, Matthey and Co. Ltd for experimental facilities and Mr J. H. F. Notton for the micro-probe analysis. We also thank Professor S. Tolansky and Dr V. I. Little for help and advice.

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Received August 27, 1970; revised April 5, 1971.

<sup>1</sup> Healy, J. F., *Congrès Intern. de Numismatique*, Actes II, 529 (1957).

<sup>2</sup> Herodotus, I, 50, 2 (λευκὸς χρυσός).

<sup>3</sup> Strabo, XI, ii, 19, and Isidorus, *Origines* XVI, xxiv.

<sup>4</sup> Pliny, *Natural History*, XXXIII, 80, and Isidorus, *ibid.* (χρυσίον ηλεκτρον, and electrum).

<sup>5</sup> *Inscriptiones Graecae*, XII (2), 1; Tod, M. N., *Greek Historical Inscriptions*, II, 112.

<sup>6</sup> Healy, J. F., *J. Hellenic Studies*, LXXVII, Part 2, 267 (1957).

<sup>7</sup> *Congrès Intern. de Numismatique*, Actes II, 533 (1957).

<sup>8</sup> Head, B. V., *Numismatic Chronicle*, 277 (1887); Hammer, J., *Zeitschrift für Numismatik*, XXVI, 1–144.

<sup>9</sup> Kraay, C. M., *Archaeometry*, 1, 6 (1958); Kraay, C. M., and Emeleus, V. M., *The Composition of Greek Silver Coins: Analysis by Neutron Activation*.

<sup>10</sup> Wroth, W. W., *British Museum Catalogue of Greek Coins, Troas, Aeolis, Lesbos*, pl. xxxiv, 5.

<sup>11</sup> *Congrès Intern. de Numismatique*, Actes II, 533 (1957).

<sup>12</sup> Hughes, M. J., and Oddy, W. A., *Archaeometry*, Part 1, 12 (1970).

<sup>13</sup> Hall, E. T., *Archaeometry*, 3, 29 (1960).

<sup>14</sup> Hall, E. T., *Archaeometry*, 4, 62 (1961).

<sup>15</sup> Hornblower, A. P., *Archaeometry*, 5, 108 (1962).

## BIOLOGICAL SCIENCES

Differences in Growth *in vitro* of Adipose Cells from Normal and Obese Patients

OBESITY is a bodily state in which an excessive accumulation of fat occurs, but it is not known whether it is the lipid content per cell<sup>1</sup> or the total number of adipose cells<sup>2</sup> which increases. Bray<sup>3</sup> found that adipose cells from obese patients were larger than those from normal patients, and concluded that the gain or loss of weight in adults occurs chiefly through changes in the size of existing fat cells. Fat cells *in vivo*, however, are greatly influenced by the nutritional state of the patients, and observations in such conditions do not indicate whether there are acquired and/or inborn differences in adipose cells from normal and obese patients.

We have therefore examined these cells for growth, size and cellular reproduction *in vitro*, where they are not affected by the nutritional state of the patients.

Subcutaneous adipose tissue was obtained from patients, aged 35–50, undergoing abdominal surgery. Cells were dispersed with collagenase according to Rodbell<sup>4</sup> and centrifuged at low speed. The sedimented cells were cultured on glass cover slips in Leighton tubes containing 1.5 ml. of lactalbumin hydrolysate growth medium supplemented with 20% foetal calf serum, in an atmosphere of 5% CO<sub>2</sub>–95% air at 37° C. One day after the establishment of the culture, the culture medium was replaced with fresh medium to remove red blood cells. The cells were then differentially stained with oil red O and Harris haematoxylin solution. The number and size of cells were evaluated respectively by direct microscopic counting and by planimetric measurement from photographs of the cells.

The cells in early cultures resembled fibroblasts and contained some lipids; after 2 months they became balloon shaped—a characteristic of adipose cells—and accumulated large amounts of lipids. In two samples from obese patients, the cultures maintained for 2 months each produced a large mass, several cell layers thick. Microscopy showed that these masses were very similar to the original adipose tissue, and contained a large quantity of lipids.

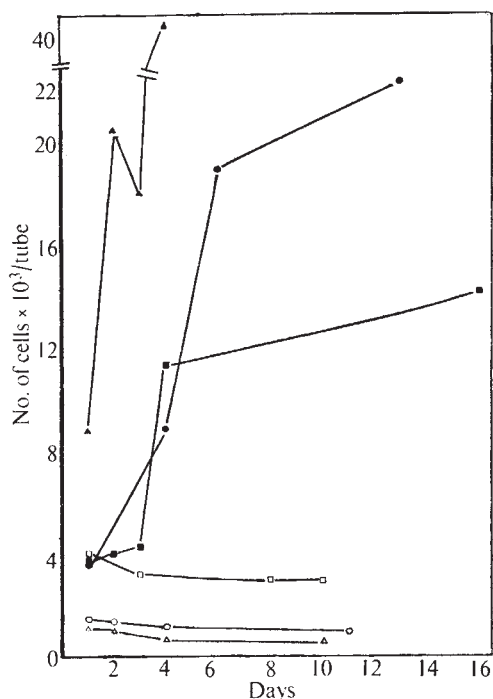


Fig. 1 The growth curves of adipose cells from normal patients: Ro,  $\Delta$ ; Hu,  $\square$ , and Fo,  $\circ$ ; and obese patients: Ma,  $\blacktriangle$ ; Si,  $\blacksquare$ , and Og,  $\bullet$ , *in vitro*.

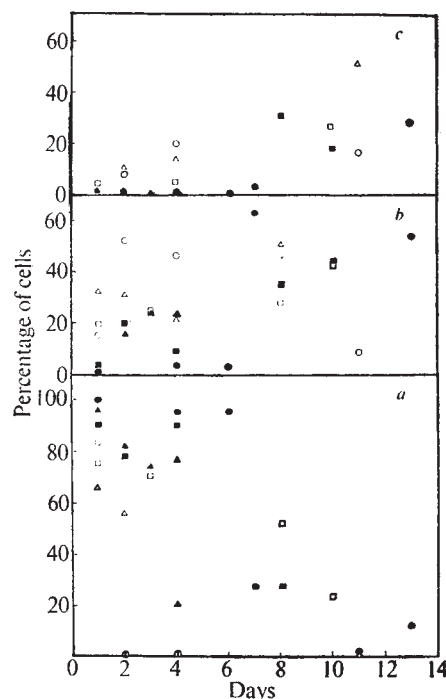


Fig. 2 The distribution of adipose cells (percentage of population) from normal patients: Ro,  $\Delta$ ; Hu,  $\square$ , and Fo,  $\circ$ ; and obese patients: Ma,  $\blacktriangle$ ; Si,  $\blacksquare$ , and Og,  $\bullet$ , in different size ranges: a, (0–0.05) inch<sup>2</sup>; b, (0.05–0.10) inch<sup>2</sup>; and c, (0.10–0.15) inch<sup>2</sup>, after magnification  $\times 32.2$ .

The results of growth of adipose cells *in vitro* (Fig. 1) from normal patients indicated no increase in cell number with time. In contrast, adipose cells from obese patients rapidly increased in number in the first 4–6 days of culture and then stopped dividing. Measurements of the size of adipose cells (Fig. 2) showed that cells from normal patients rapidly increased in size with time, whereas cells from obese patients did not increase in size until they reached the stationary phase.

The study of the effect of hormones and other growth factors on the cellular growth and reproduction of adipose cells in culture may give further information on the peculiarities of these cells. These aspects are currently being investigated.

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<sup>1</sup> Sims, E. A. H., Goldman, R. F., Gluck, C. M., Horton, E. S., Kellcher, P. C., and Horton, E., in *Physiopathology of Adipose Tissue* (edit. by Vague, V.) (Excerpta Medica Foundation, Amsterdam, 1969).

<sup>2</sup> Hirsch, J., Knittle, J. L., and Salans, L. B., *J. Clin. Invest.*, **45**, 1023 (1966).

<sup>3</sup> Bray, G. A., *Amer. Coll. Physicians Fifty-second Ann. Session* (1970).

<sup>4</sup> Rodbell, R., *J. Biol. Chem.*, **239**, 375 (1964).

## Conformation of Synthetic Polypeptide Monolayers

PROTEINS and synthetic polypeptides spread at air/water interfaces are thought to exist in extended chain conformations<sup>1,2</sup>. From the results of deuterium exchange in monolayers, and infrared spectroscopy and electron diffraction on collapsed films, Malcolm<sup>3–5</sup> reported that the  $\alpha$ -helical



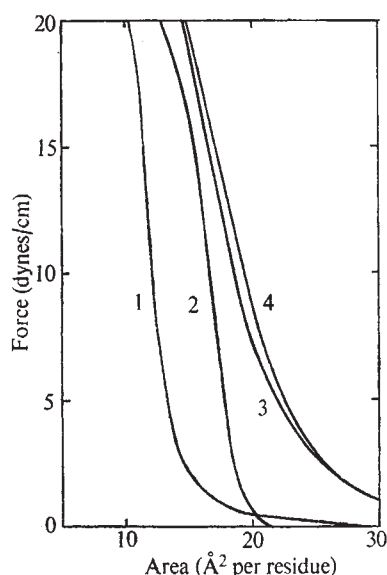


Fig. 1 The force-area curves for poly-L-alanine (curve 1), poly-L-leucine (2), poly-L-valine (3), and poly-L-isoleucine (4).

conformation is stable in synthetic polypeptide monolayers. From the relationship between the temperature coefficient of monolayer transition pressure and the content of regular helix in the solid state, Yamashita and Yamashita<sup>6</sup> reached a similar conclusion for poly- $\gamma$ -benzyl glutamates.

Poly-L-valine and poly-L-isoleucine seem to be relatively unstable in the  $\alpha$ -helical conformation in the solid state<sup>7,8</sup>, compared with poly-L-alanine and poly-L-leucine. I report here corresponding differences in the monolayer properties of these polymers.

The polymers examined were: poly-L-alanine (0.91); poly-L-leucine (0.85); poly-L-valine (0.23); and poly-L-isoleucine (0.20). The reduced viscosity in dl g<sup>-1</sup> measured at 0.2% concentration in trifluoroacetic acid (TFA) at 25° C is given in brackets. Spreading solutions were made by dissolving the polymer (2.5 mg) in TFA (10 ml.), in which all the polymers investigated were in the random form<sup>7</sup>. The spreading solution was deposited onto the surface of twice distilled water from a micrometer syringe. The initial spreading area was 55 Å<sup>2</sup> per residue. The trough (60 × 15 × 1 cm) and compressing barriers were made of 'Teflon'. The film was compressed at a rate of 2 mm min<sup>-1</sup> (0.2 Å<sup>2</sup> per residue per min). The surface pressure was measured by the Wilhelmy method.

Fig. 1 shows the force-area curves for poly-L-alanine, poly-L-leucine, poly-L-valine and poly-L-isoleucine. Clearly there is a difference between the monolayers of poly-L-alanine and poly-L-leucine and of poly-L-valine and poly-L-isoleucine. The extrapolated limiting areas for poly-L-alanine and poly-L-leucine are about 13.5 Å<sup>2</sup> per residue and 19 Å<sup>2</sup> per residue, respectively. Both polymers yield condensed monolayers, but those of poly-L-valine and poly-L-isoleucine are expanded, giving extrapolated areas of about 22 Å<sup>2</sup> per residue and 23 Å<sup>2</sup> per residue, respectively. No significant difference was observed between the monolayers spread from solutions in TFA and in TFA-chloroform mixed solvent (40 v/v % chloroform for poly-L-alanine; 60 v/v % chloroform for poly-L-leucine) in which the polymers are  $\alpha$ -helical<sup>9</sup>.

Malcolm<sup>4</sup> suggested that there are three types of possible conformations for the patterns of hydrogen-bonding: (1) monolayers in which the peptide groups are hydrogen bonded intramolecularly, as in  $\alpha$ -helix; (2) extended chain conformations with intermolecular hydrogen bonds, as in  $\beta$ -keratin; (3) extended chains with hydrogen bonds between amide groups and water molecules in the environment, which have increased flexibility compared with (1) and (2).

The results obtained here clearly indicate that the conformations of poly-L-alanine and poly-L-leucine and of poly-L-valine

and poly-L-isoleucine differ in the monolayer state as in the solid state. The limiting areas per residue for poly-L-alanine and poly-L-leucine agree closely with those reported for poly-D-alanine and poly-DL-leucine<sup>4,5</sup>. Possibly these polymers are  $\alpha$ -helical, or predominantly  $\alpha$ -helical, even in monolayers. The force-area curves show that poly-L-valine and poly-L-isoleucine are more flexible than the other two polymers, and may therefore have structures of type (3). The observed areas for poly-L-valine and poly-L-isoleucine are consistent with an extended chain structure, with the side chains in the water surface directed alternately on either side of the molecule. If there is no appreciable interpenetration of the side chains, the observed areas are reasonable, and significantly higher than for the  $\alpha$ -helical structure as I suggest for poly-L-leucine, and as reported for poly-DL-leucine (17.5 Å<sup>2</sup>) and poly-L-norvaline (17.0 Å<sup>2</sup>)<sup>5</sup>.

I thank Mr Shinsuke Yamashita and Mr Naokuni Yamawaki, Department of Polymer Science, Osaka University, for poly-L-alanine, poly-L-valine and poly-L-isoleucine. This research was partly supported by a grant from the Ministry of Education.

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- <sup>1</sup> Bull, H. B., *Adv. Protein Chem.*, **3**, 95 (1947).
- <sup>2</sup> Cheesman, D. F., and Davies, J. T., *Adv. Protein Chem.*, **9**, 439 (1954).
- <sup>3</sup> Malcolm, B. R., *Nature*, **195**, 901 (1962).
- <sup>4</sup> Malcolm, B. R., *Surface Activity and Microbial Cell*, 102 (Soc. of Chem. Ind., London, 1965).
- <sup>5</sup> Malcolm, B. R., *Proc. Roy. Soc., A*, **305**, 363 (1968).
- <sup>6</sup> Yamashita, T., and Yamashita, S., *Bull. Chem. Soc. Jap.*, **43**, 3969 (1970).
- <sup>7</sup> Blout, E. R., *Polyamino Acids, Polypeptides and Proteins*, 275 (edit. by Stahman, M. A.) (University of Wisconsin Press, Madison, 1962).
- <sup>8</sup> Fraser, R. D. B., Harrap, B. S., MacRae, T. P., Stewart, F. H. C., and Suzuki, E., *J. Mol. Biol.*, **12**, 482 (1965).
- <sup>9</sup> Fasman, G. D., *Polyamino Acids, Polypeptides and Proteins*, 221 (edit. by Stahman, M. A.) (University of Wisconsin Press, Madison, 1962).

## Absence of Histone in the Blue-Green Alga *Anabaena cylindrica*

THE finding that more histones are associated with the chromosomal DNA of higher organisms than with that of lower organisms<sup>1-4</sup> is consistent with the suggestion<sup>5</sup> that histones act as suppressors in the regulation of gene expression in cellular differentiation. Thus histones must have been acquired at some stage in the evolution of differentiated eukaryotic organisms from the primitive prokaryon.

Blue-green algae, like bacteria, lack a nuclear membrane; but their mode of photosynthesis strongly resembles that of the eukaryotic algae and higher plants, and phycocyanin and phycoerythrin, the photosynthetic pigments of blue-green algae, are also characteristic of red algae and other small groups. Blue-green algae are thus of considerable phylogenetic interest; we here report our analysis of the protein components of the chromosomes of *Anabaena cylindrica*.

Cells were grown in modified Detmer's medium<sup>6</sup> at 25° C and continuously aerated with filtered air containing 0.1% CO<sub>2</sub> and illuminated with tungsten lamps at 600-1,500 lux. Cells were collected at the late linear phase and repeatedly washed before being frozen in liquid nitrogen. The stocked cells were ground with 3 w/w quartz sand in a precooled mortar at 4° C. The soluble components were then extracted with 4 volumes of the extraction buffer (0.05 M NaCl-0.005 M MgCl<sub>2</sub>-0.05 M Tris-HCl, pH 7.5), followed by low speed

centrifugation to remove whole cells and sand. The extract was spun at 25,000g for 20 min to remove large particles before being subjected to ultracentrifugation at 105,000g for 90 min to sediment out the microsomes and membrane fractions. The supernatant, a reddish-purple solution, was finally centrifuged at 150,000g for 5 h. The resultant purple sticky pellet was mildly dispersed into the extraction buffer minus magnesium chloride and dialysed against the same buffer. It was then subjected to electrophoresis in starch or 'Pevicon C870' block equilibrated with the same buffer and filled in a 3 × 6 × 40 cm acryl trough, in which the sample solution was charged 8 cm off the anodal end. Electrophoresis was performed in a cold room at constant current of 40 mA for 48 h. After partial extraction from small blocks along the trough, the algal deoxy-ribonucleoprotein (DNP) region was determined by 260 nm absorption and from the corresponding region, the bulk crude DNP was extracted, followed by concentration in a collodion bag to several ml. The concentrated crude DNP was treated with RNAase (50 µg/ml.) at 4° C for 1 h before gel filtration through a 'Sephadex G-200' column equilibrated with the same buffer to remove free proteins of relatively low molecular weight as well as fragmented RNAs. The DNP was recovered in an eluate just after the initial void volume and pooled to be used as the final preparation of the purified DNP.

The chemical composition of the purified DNP was determined according to the methods of Burton, Meibbaum and Lowry, respectively, giving the ratio: DNA 88, RNA 4 and protein 8. This ratio is quite different from that of any eukaryotic cells ever examined, but is similar to that of bacteria<sup>7</sup>. For the detection of histones, the purified DNP preparation was treated with 0.1 M H<sub>2</sub>SO<sub>4</sub> and the extracted protein was precipitated with 80% cold ethanol. The percentage of acid-extractable protein in the three experiments was 36.5, 18.7, or 25.5 of the whole DNP protein, respectively, giving the average value of 26.9%. Then the acid-extractable protein was dissolved in 10 M urea to a concentration of approximately 150 µg/ml. and analysed by acryl amide gel disk electrophoresis at pH 4.3 with a parallel run of calf-thymus histone for reference. In spite of the fact that enough protein was loaded, no detectable band could be observed after amidoblack staining, whereas calf-thymus histone in these conditions would normally separate into several components. This may mean that the basicity of the acid-extractable protein was rather weak, although it was barely soluble in acid. A similar observation has been reported on a mould acid-extractable DNP (ref. 3). Finally, to ascertain the basicity, amino-acid composition of the acid-extractable protein was analysed by an automatic amino-acid analyser. The result gave the molar ratio of basic amino-acids (His, Lys, Arg) to acidic ones (Asp, Glu) of 0.9, showing that the acid-extractable protein was neutral.

The chromosomes of *Anabaena cylindrica* therefore contain a small amount of acid-extractable protein, which, however, is not as strongly basic as the histones of eukaryotic cells. There should be little loss of chromosomal basic protein during the purification procedure in the experimental conditions, pH and ionic strength, which were chosen so as to maintain the integrity of DNP. Our results agree with electron microscopic observations of Leak<sup>8</sup>, who demonstrated the presence of fine fibrils in the nucleoplasm of some blue-green algae and suggested low chromosomal protein content. We have confirmed this in *Anabaena* cells in which we found that the nucleoplasm consisted of unit fibrils with a diameter of 30 Å and their aggregated form.

We thank Dr T. Shiroya for his encouragement, and Dr H. Matsushima and Miss I. Uesugi for their technical assistance.

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- <sup>1</sup> Zubay, G., and Watson, M. R., *J. Biophys. Biochem. Cytol.*, **5**, 55 (1959).
- <sup>2</sup> Dwivedi, R. S., Dutta, S. K., and Bloch, D. P., *J. Cell Biol.*, **43**, 51 (1969).
- <sup>3</sup> Tonimo, G. J. M., and Rozin, Th. H., *Biochim. Biophys. Acta*, **124**, 427 (1966).
- <sup>4</sup> Mita, T., Shiomi, H., and Iwai, K., *Exp. Cell Res.*, **43**, 696 (1967).
- <sup>5</sup> Stedman, E., and Stedman, E., *Nature*, **166**, 780 (1950).
- <sup>6</sup> Watanabe, A., *J. Gen. Appl. Microbiol.*, **6**, 283 (1960).
- <sup>7</sup> Kadoya, M., Mitsui, H., and Takagi, Y., *Biochim. Biophys. Acta*, **91**, 36 (1964).
- <sup>8</sup> Leak, L. V., *J. Ultrastruct. Res.*, **20**, 190 (1967).

## Inhibition of Carcinogenesis by Dietary Zinc

We are prompted by two recent publications to communicate incomplete results of an experiment which is still in progress. Levij and Polliack<sup>1</sup> reported the inhibition of chemical carcinogenesis in the hamster cheek pouch by topical application of chlorpromazine; DeWys *et al.*<sup>2</sup> reported the inhibition of Walker 256 carcinosarcoma growth by dietary zinc deficiency. We have achieved a result similar to that of Levij and Polliack by a method diametrically opposite to that of DeWys *et al.*: we have inhibited carcinogenesis in the hamster cheek pouch by the administration of additional zinc.

Our experiments were designed to examine the effect of substances which promote healing on the course of DMBA-induced carcinoma in the hamster cheek pouch, either intact or previously subjected to a standardized wound. Orally administered zinc sulphate, at a dose of 220 mg t.i.d., has been shown to have a pronounced effect in accelerating the healing of wounds in young, healthy human subjects<sup>3</sup>. Zinc has also been shown to be preferentially concentrated in healing tissues, peak levels being reached on the third day after injury<sup>4</sup>.

In that part of our experiments reported here, forty young Syrian golden hamsters were divided into three groups of ten, ten and twenty, matched for weight and sex. Losses due to unrelated causes reduced these groups to nine, nine and fifteen. All animals were maintained on MRC 41B pellet diet which contains 21.9 p.p.m. of zinc. One group of ten received 100 p.p.m. of Analar zinc sulphate in the drinking water. Ten animals in the second group, anaesthetized with intraperitoneal Nembutal, were subjected to a standardized injury 2 cm in diameter in the right cheek pouch by means of electrocautery. Four days later, and three times weekly for the next 4 weeks, the right cheek pouch of each animal was painted with 0.5% solution of DMBA in liquid paraffin. After 4 weeks no further carcinogen was applied and thereafter the animals were examined regularly under light ether anaesthesia and their body weight was checked.

**Table 1** Tumour Growth during Administration of Dietary Zinc

| Six month observations |                |                                         |                               |
|------------------------|----------------|-----------------------------------------|-------------------------------|
|                        | No. of animals | Weeks before appearance of first tumour | No. of tumour-bearing animals |
| Control group          |                |                                         |                               |
| DMBA only              | 15             | 9                                       | 13 (87%)                      |
| Electrocautery + DMBA  | 9              | 9                                       | 6 (66%)                       |
| Zinc 100 p.p.m. + DMBA | 9              | 25                                      | 1 (11%)                       |

The administration of zinc as a dietary supplement seems to exert an inhibitory effect on tumour formation (Table 1). Animals which had not received the zinc supplement but whose pouches had been injured were less protected against the effect of DMBA but markedly less susceptible than the control



group. In view of the localization of zinc at the site of an injury it seems possible that some protection has been afforded at the site of application of the carcinogen.

Recognizing the long latent period sometimes observed in carcinogenesis we have allowed this experiment to continue, and after 10 months there has been no increase in tumour formation in the animals receiving zinc solution (to which thymol in trace amounts has since been added to suppress the growth of moulds). At the end of the 10 month period five surviving animals of the group receiving zinc are still free of tumour growth.

Aspects of this experiment still to be reported include several permutations of the groups mentioned above as well as a long-term study on C3H mice in which a high proportion of females develop spontaneous mammary cancer.

We thank Dr C. P. Geary for assistance during his tenure of a Nuffield Travelling Fellowship in the department.

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<sup>1</sup> Levij, I. S., and Polliack, A., *Nature*, **228**, 1096 (1970).

<sup>2</sup> DeWys, W., Pories, W. J., Richter, M. C., and Strain, W. H., *Proc. Soc. Exp. Biol. Med.*, **135**, 17 (1970).

<sup>3</sup> Pories, W. D., Henzel, J. H., Rob, C. G., and Strain, W. H., *Lancet*, **i**, 121 (1967).

<sup>4</sup> Savlov, E. D., Strain, W. H., and Huegin, F., *J. Surg. Res.*, **2**, 209 (1962).

## SV40 Neutralizing Antibodies in Sera of US Residents without History of Polio Immunization

SIMIAN virus 40 (SV40) is a natural infection of rhesus and some other Asiatic macaques<sup>1</sup> and has no known natural host in the United States. It is therefore difficult to account for our find-

ing of antibodies neutralizing SV40 in the sera of some elderly persons in the United States who do not have a history of immunization with any vaccine prepared in rhesus kidney cultures. The only recognized exposure of the US population to this virus occurred when poliovirus and adenovirus vaccines prepared in rhesus kidney cultures and administered to a large number of people were later found to have been contaminated with SV40 (ref. 1). The chief exposure occurred between 1955 and 1961 through the use of Salk vaccine, and it is known that subcutaneous administration of SV40 gives a long-lasting antibody response<sup>2</sup>.

We made our observations during a continuing study of cancer of the urinary bladder in a search for possible papovavirus aetiology. Sera from 210 patients with bladder or other types of cancer were screened for antibodies to SV40. The donors comprised 157 white males, thirty-seven white females, fifteen negro males and one negro female and had a median age of 66.

The sera were initially screened at 1 : 2 dilution in SV40 virus neutralization tests<sup>3</sup>. Antibodies were detected in sera of two of eight Salk vaccinees and in seven of 184 who gave a history of no immunization. These latter seven donors, six white males and one white female, were interviewed in detail about their immunization history and were bled periodically for antibody determination in neutralization, fluorescent antibody<sup>4</sup> and radioisotope precipitation (RIP) tests<sup>5</sup>.

All seven affirmed that they had not received any kind of poliovaccine. Detailed questioning provided no evidence that any of them was either immunized with an experimental vaccine or was exposed to a known source of SV40 in his occupation or travel. Antibody levels in different bleedings of the same individual were comparable (Table 1). Neutralizing antibody titres in different individuals ranged from 1 : 2 to 1 : 64. Sera from four persons specifically and consistently stained SV40 viral antigen in indirect fluorescent antibody tests. With the exception of sera from C. D., which had titres of 1 : 16 and 1 : 32, antibody titres in fluorescent antibody tests were low. None of the approximately 200 neutralization negative sera stained the viral antigen, thus indicating the specificity of the reaction. None of the sera, including those from C. D., stained SV40 T antigen. The results of RIP tests generally supported the neutralization and fluorescent antibody studies. The sera

Table 1 Presence of SV40 Antibodies in Sera of Cancer Patients

| Patient | Age | Sex | Date of bleeding | Neutral. anti-body titre | SV40 antibodies          |                                       | RIP value |         | Diagnosis and status of disease                  |
|---------|-----|-----|------------------|--------------------------|--------------------------|---------------------------------------|-----------|---------|--------------------------------------------------|
|         |     |     |                  |                          | FA-viral anti-body titre | (% virus precipitated) serum dilution | 1 : 20    | 1 : 100 |                                                  |
| N. H.   | 68  | M   | 6-21-69          | 1 : 8                    | 1 : 2                    | 27                                    | 16        |         | Carcinoma prostate, treated June and August 1969 |
|         |     |     | 9-17-69          | 1 : 8                    | 1 : 4                    | 33                                    | 14        |         |                                                  |
|         |     |     | 4-13-70          | 1 : 2                    | 1 : 1                    | 24                                    | —         |         |                                                  |
| C. D.   | 56  | M   | 6-10-69          | 1 : 8                    | 1 : 32                   | 46                                    | 16        |         | Treated carcinoma bladder. No recurrence, 1 yr   |
|         |     |     | 9- 9-69          | 1 : 8                    | 1 : 32                   | 49                                    | 17        |         |                                                  |
|         |     |     | 5-26-70          | 1 : 4                    | 1 : 16                   | 55                                    | —         |         |                                                  |
| L. G.   | 66  | M   | 5-24-69          | 1 : 8                    | Negative                 | —                                     | 5         |         | Treated carcinoma bladder. No recurrence, 4 yr   |
|         |     |     | 9-17-69          | 1 : 4                    | Negative                 | 5                                     | 3         |         |                                                  |
| H. G.   | 69  | M   | 6-26-69          | 1 : 16                   | 1 : 1                    | 29                                    | 13        |         | Treated carcinoma bladder. No recurrence, 5 yr   |
|         |     |     | 8-24-69          | 1 : 32                   | 1 : 1                    | 26                                    | 14        |         |                                                  |
|         |     |     | 3-10-70          | 1 : 32                   | 1 : 1                    | 18                                    | —         |         |                                                  |
| W. C.   | 50  | M   | 6-22-69          | 1 : 4                    | Negative                 | 6                                     | 6         |         | Treated seminoma testes. No recurrence, 3 yr     |
|         |     |     | 5-26-70          | 1 : 4                    | Negative                 | 7                                     | —         |         |                                                  |
| C. C.   | 58  | F   | 9-12-69          | 1 : 64                   | 1 : 8                    | 62                                    | 25        |         | Follicular lymphosarcoma. Treated October 1969   |
|         |     |     | 2-18-70          | 1 : 64                   | 1 : 2                    | 24                                    | —         |         |                                                  |
| G. H.   | 74  | M   | 1-29-70          | 1 : 32                   | Negative                 | 10                                    | —         |         | Carcinoma prostate, persistent, 3 yr             |
|         |     |     | 6- 5-70          | 1 : 32                   | Negative                 | 19                                    | —         |         |                                                  |

Antibodies to SV40 in repeated bleedings of seven individuals without history of poliovirus immunization. Results of only some of the collected sera are given. A serum was interpreted as staining SV40 viral antigen in fluorescent antibody tests if (a) there was nuclear fluorescence of at least 1+ intensity in the appropriate proportion of cells; (b) the serum did not stain uninfected cells; and (c) the staining was inhibited by previous treatment of the cultures with FUDR. For determination of T antibodies, sera were reacted against SV40-transformed hamster cells and against FUDR-treated acutely infected cells. An RIP value (% virus precipitated) of 12% was considered positive. Eleven neutralization negative sera had RIP values of 0-6%. A hyperimmune monkey anti-SV40 serum gave 60-80% precipitation.

of N. H., C. D., H. G., and C. C., at 1 : 20 dilution consistently gave precipitation values well above the 12% used in the past to define a positive serum<sup>6</sup>. These sera were also positive in both neutralization and fluorescent antibody tests. In all cases tested, sera which were positive at 1 : 20 dilution were also positive at 1 : 100 dilution, though with lower values (Table 1).

The evidence for the presence of SV40-reacting antibodies in most of the individuals listed in Table 1 is unequivocal. These included patients with different malignant diseases, active or inactive. Other preliminary studies do not suggest a higher prevalence of antibodies in patients with cancer of the bladder than in any other diagnostic category<sup>7</sup>. Although it is impossible to exclude the possibility that the donors, in spite of their history, were immunized with Salk vaccine, several considerations make this unlikely. It has been estimated that only about 10% of the non-institutionalized civilian population aged 50–59 yr had received one or more inoculations of Salk vaccine by September 1961 (ref. 8); the median age of our subjects was 58 yr in 1961. Furthermore, not all lots of Salk vaccine were contaminated with SV40 (ref. 9) and not all people who received contaminated vaccine uniformly developed SV40 antibodies<sup>1,2</sup>.

In earlier investigations<sup>3,4</sup>, one of us reported the detection of SV40 neutralizing antibodies in sera of normal and cancerous individuals in North India not immunized with polio-vaccine and had interpreted this to indicate natural transmission of SV40 from the resident rhesus population to man. Although this interpretation may still be correct, our findings, as well as the recent detection of SV40 antibodies in human sera from South India where rhesus is not prevalent<sup>6</sup>, raise the possibility of alternative explanations. The antibodies may be the result of infection with a related papovavirus. Papovaviruses known to infect man include the wart virus and the virus seen by electron microscopy in lesions of progressive multifocal leucoencephalopathy<sup>10</sup>. There are also reports of isolation of papova-like viruses from human brains of Creutzfeld-Jacob disease<sup>11</sup> and subacute sclerosing panencephalitis<sup>12</sup>. It is not known whether infection with any of these agents will produce antibodies which will react with SV40 virion. There may be natural hosts of SV40 other than Asiatic macaques or the antibodies may be a result of infection with a hitherto undescribed SV40-like infection of man.

This work was supported by grants from the American Cancer Society, the National Institutes of Health and the National Chapter of Phi Beta Phi Sorority.

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- <sup>5</sup> Ozer, H. L., Takemoto, K. K., Kirschstein, R. L., and Axelrod, D., *Virology*, **3** (1), 17 (1969).
- <sup>6</sup> Shah, K. V., Goverdhan, M. K., and Ozer, H. L., *Amer. J. Epidemiol.*, **93**, 291 (1971).
- <sup>7</sup> Shah, K. V., Palma, L. D., and Murphy, G. P., *J. Surg. Oncol.*, **3** (in the press).
- <sup>8</sup> CDC, *USPHS, Polio Surveillance Reports*, Report No. 248, 5 (1961).
- <sup>9</sup> Gerber, P., Hottle, G. A., and Grubbs, R. E., *Proc. Soc. Exp. Biol. Med.*, **108**, 205 (1961).
- <sup>10</sup> Zu Rhein, G., *Prog. Med. Virol.*, **11**, 185 (1969).
- <sup>11</sup> Vernon, M. L., Fuccillo, D. A., and Hamilton, R., *Fed. Proc.*, **29**, No. 229 (1970).
- <sup>12</sup> Koprowski, H., Barbanti-Brodano, G., and Katz, M., *Nature*, **225**, 1045 (1970).

## Feedback Regulation of Growth of Ascites Tumours in Parabiotic Mice

ALTHOUGH continuous growth is a characteristic feature of most malignant tumours, the experimental ascites tumour is quite different. From the moment of inoculation, its growth rate decreases at a constant rate, the number of tumour cells usually reaching a plateau before the death of the host. At this point, cell renewal equals cell loss. This growth inhibition has been explained in terms of a deficient nutrient supply, an accumulation of toxic metabolites or oxygen deficiency, and no doubt these conditions do influence the growth rate of the tumour, but there are reasons to believe that other mechanisms are important.

Brown<sup>1</sup> inoculated two different ascites tumours, the Ehrlich hypotetraploid ascites carcinoma, line E-2, and the Crocker ascites sarcoma, in the same mouse. Counts of the tumour cells demonstrated that the tumours developed independently. They grew in a completely additive fashion for the first 5 days after inoculation and in a partially additive fashion 9 and 14 days after challenge. Thus the plateau phenomenon in mice bearing one ascites tumour can hardly be explained by a nutrient exhaustion or by accumulation of metabolic products.

Aspiration of most of the tumour from mice bearing ascites tumours at the plateau was followed 24 h later by a marked increase in the growth rate (the secondary or recurrent growth) determined by means of 'Colcemid' (ref. 2) or by means of <sup>3</sup>H-thymidine incorporation in the DNA of the tumour cells<sup>3</sup>. Furthermore, there was a pronounced inhibition of this second growth after injection of cell-free ascites, obtained from mice bearing fully developed ascites tumours, into mice with ascites tumours in the recurrent phase of growth<sup>2</sup>. These results indicate that the rate of growth of the ascites tumours depends in some way on the amount of tumour tissue present in the mouse, a situation similar to the regulation of growth of the normal tissue.

In our experiments a transplantable plasmacytoma, JB-1, was used. The tumour appeared spontaneously in our inbred AK-A strain of mice in 1950 and it has been maintained syngeneically as a solid as well as an ascites tumour. AK-A mice about 2 months old were joined in parabiosis (brother-brother or sister-sister) without opening the peritoneal cavities. If signs of parabiotic intoxication appeared, the animals in question were excluded from the experimental material. Both members of a pair of parabiotic mice were inoculated intraperitoneally with 10<sup>7</sup> JB-1 ascites tumour cells. Only in about 30% of cases did ascites tumours develop in both mice although 10<sup>7</sup> JB-1 cells is ten times the dose necessary for the development of an ascites tumour in 100% of single mice.

The phenomenon of one tumour suppressing the growth of another was re-established in mice simultaneously inoculated with subcutaneous and intraperitoneal JB-1 ascites tumour cells. The subcutaneous tumour does not grow until aspiration of the ascites tumour.

<sup>1</sup> Sweet, B. H., and Hilleman, M. R., *Proc. Soc. Exp. Biol. Med.*, **105**, 420 (1960).

<sup>2</sup> Gerber, P., *Proc. Soc. Exp. Biol. Med.*, **125**, 1284 (1967).

<sup>3</sup> Shah, K. V., *Proc. Soc. Exp. Biol. Med.*, **121**, 303 (1966).

<sup>4</sup> Shah, K. V., *J. Nat. Cancer Inst.*, **42**, 139 (1969).



Although the mice selected for a parabiotic pair were as similar as possible, there were probably small differences, for example, in the growth rate of an ascites tumour, that may have caused one tumour to inhibit the other. Only in the situations where the two tumours have almost equal conditions will normal development of the ascites tumours in both mice of the parabiotic pair take place.

When one mouse of the pair had a fully developed ascites tumour, and the partner had a small one, the mouse bearing the large tumour was subjected to aspiration 10 days after the inoculation at the beginning of the plateau. The mitotic index (MI) (percentage of tumour cells in mitosis, found by counting 1,000 cells in smears) increased after 24 h in both mice (Fig. 1, upper part). When both mice had large tumours, one was subjected to aspiration 10 days after inoculation. No increase in the MI occurred after 24 h in any of the mice (Fig. 1, lower part). The same two groups were investigated 24 h after aspiration by intraperitoneal injection of 'Colcemid' (1 mg/kg mouse, Fig. 2).

It seems that the non-aspirated, fully developed ascites tumour exerts a retarding effect on the recurrent growth of the tumour subjected to aspiration. This could be explained by a diffusion through the peritoneum into the circulation of the inhibiting principle found in the cell-free ascites fluid of the fully developed ascites tumours. The nature of this inhibiting principle is unknown, but it is tempting to draw a parallel between the growth regulation of this malignant system and normal growth regulation. Several normal tissues are known to be restrained from unlimited growth by a negative feedback mechanism.

Much attention has been paid recently to the chalones<sup>4</sup>, which are tissue specific humoral mitotic inhibitors which seem to regulate the growth rate of some normal tissues. A defect in the chalone regulation has been sought as the reason for unrestricted growth of the cancer. What has been found is a decrease in the intracellular content of chalone from 1/10 to 1/40 of the normal<sup>5,6</sup>, an increase in the concentration of

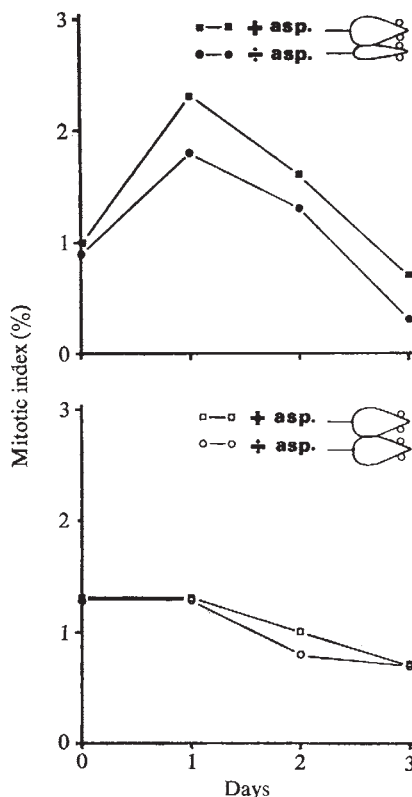


Fig. 1 Mitotic index (ordinate) of JB-1 ascites tumour in parabiotic mice (mean of three pairs) against days after the aspiration (abscissa).

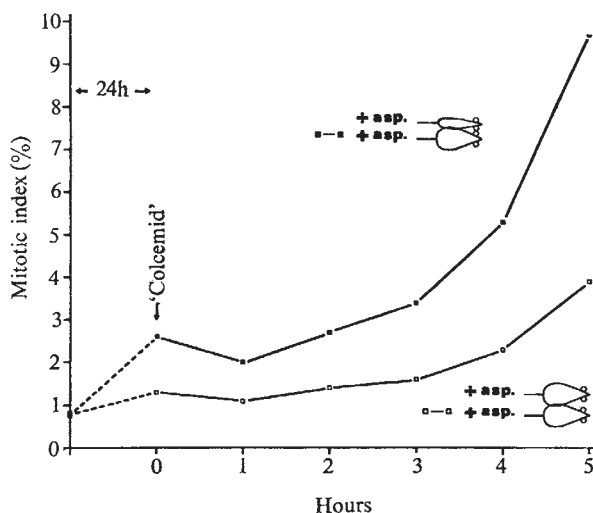


Fig. 2 Percentage of mitotic tumour cells of JB-1 ascites tumours in parabiotic mice determined by means of 'Colcemid' on the day after the aspiration.

chalone in the serum<sup>6</sup> and, in comparison with the sensitivity of normal cells, a decreased sensitivity of the malignant cells to the chalones<sup>6</sup>. The difference between these results and the experiments with the ascites tumours is that the latter reach the point of balance while the hosts are still in acceptable conditions. Most other cancers kill their hosts before reaching this point. The specificity of the tumour inhibiting principle is under investigation.

This work was supported by the Danish Cancer Society and the Carl Schepler and Wife's Bequest of the Irma Foundation.

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- <sup>1</sup> Brown, H. R., *Anat. Rec.*, **166**, 283 (1970).
- <sup>2</sup> Bichel, P., *Europ. J. Cancer*, **6**, 291 (1970).
- <sup>3</sup> Burns, E. R., *Cancer Res.*, **28**, 1191 (1968).
- <sup>4</sup> Bullough, W. S., and Laurence, E. B., *Proc. Roy. Soc., B*, **151**, 517 (1960).
- <sup>5</sup> Bullough, W. S., and Laurence, E. B., *Europ. J. Cancer*, **4**, 587 (1968).
- <sup>6</sup> Rytömaa, T., and Kiviniemi, K., *Europ. J. Cancer*, **4**, 595 (1968).

## Neonatal Thymectomy and Non-viral Mammary Tumours in Mice

IMMUNE responses often delay or prevent tumour induction by chemical carcinogens and oncogenic viruses<sup>1-9</sup>. Immune deficits, particularly of cellular immune responses, result in an increased frequency of neoplasms or a shortened latent period or both, and there is evidence<sup>10-12</sup> for a delayed but distinct decrease in immune reactivity to some antigens with advancing age after the removal of the thymus, even in the adult, which emphasizes that the thymus has a continuing influence on immunological responses throughout life. No systematic study has been reported of the effect of induced immune defects (by neonatal thymectomy or by antilymphocyte serum, for example) on the frequency of spontaneous neoplasms of old age. We present the results of the influence of early thymectomy on the frequency of spontaneous neoplasms of several types in two groups of mice.

C57BL/KaLw strain mice and an F<sub>1</sub> hybrid obtained by mating female C57BL/KaLw with male C3Hf/HeLw and

**Table 1** Influence of Neonatal Thymectomy on the Frequency of Neoplasms in BC3HF<sub>1</sub> Mice

| Group<br>(Females) | No. | Frequency and age to necropsy of mice bearing: |                       | Reticulum cell sarcomas * |
|--------------------|-----|------------------------------------------------|-----------------------|---------------------------|
|                    |     | Mammary tumours                                | Hepatomas             |                           |
| Thymectomized †    | 50  | 20 (40%)—22 1/2 months                         | 2 (4%)—20 months      | 13 (26%)—20 1/2 months    |
| Intact             | 25  | 1 (4%)—23 months                               | 2 (8%)—22 1/3 months  | 5 (20%)—25 3/4 months     |
| (Males)            |     |                                                |                       |                           |
| Thymectomized ‡    | 50  | None                                           | 8 (16%)—22 3/4 months | 11 (22%)—20 1/3 months    |
| Intact             | 31  | None                                           | 5 (16%)—25 1/2 months | 5 (16%)—22 3/4 months     |

\* Principally of type A morphology (Dunn<sup>23</sup>).

† One female (23 months) had an epithelioma in addition to RCS; one female (20 months) developed a malignant mesothelioma; five females (20–27 months) had associated mammary tumours and RCS; one female (21 months) had a mammary tumour and hepatoma.

‡ Two males (20, 20 1/2 months) presented fibrosarcomas in addition to RCS; one male (15 1/2 months) had carcinoma of the liver and one male (20 1/2 months) had a lung carcinoma in addition to an RCS.

designated (BC3HF<sub>1</sub>) all from our breeding colonies, were thymectomized at 3 days of age. A sample of sham-thymectomized at this age did not differ from intact controls and both groups are considered within the intact groups. All mice which presented neoplasms or died were necropsied and tissues taken for histologic study. Those thymectomized animals which showed residual thymic tissue were discarded from the study.

As has been found before<sup>9</sup>, the deficits created by 3 day thymectomy are subtle, but great enough to render resistant C57BL mice susceptible to the oncogenic effects of polyoma virus and to accept Y-histoincompatible skin grafts. No significant differences were found in age to death between thymectomized and intact mice which died from non-neoplastic causes nor were any differences noted in body weights taken periodically through 15 months of age. There was observed a slight reduction in total peripheral leucocytes at all ages studied through 18 months and a lymphocyte depletion to 30–50% of normal levels.

Immune responsiveness was studied in thymectomized and intact mice aged 9–20 months. Haemolysin titres, but not haemagglutination titres, to sheep red blood cells were significantly lower at all ages in the thymectomized group. Intact and thymectomized mice at 9 and at 20 months of age, immunized with human serum albumin (HSA) and skin tested intradermally<sup>13</sup>, developed oedema and erythema after 3 h followed by induration after 24 h but no significant differences were found between the groups.

A strikingly increased frequency of late occurring mammary tumours, the result of early thymectomy, was observed in female BC3HF<sub>1</sub> mice (Table 1). These mice do not carry the mammary tumour virus (MTV), for the C3Hf parent is virus-free, yet thymectomy increased the frequency to 40% from a frequency of 4% in intact females. Heston *et al.*<sup>14</sup> have recorded a similar frequency and age to death in intact BC3HF<sub>1</sub> mice, either virgins or breeders. The MTV-free mammary tumours of these thymectomized BC3HF<sub>1</sub> mice appeared as early as 20 months and as late as 33 months and ranged histologically from well differentiated papillary adenocarcinoma to anaplastic carcinomas that infiltrated into a fibrous stroma. According to Dunn's classification<sup>15</sup> the twenty neoplasms were found to be nearly equally divided among the type A, type B, and adenocanthoma groups.

Neither the frequency nor the latent period of the two other commonly occurring spontaneous neoplasms of BC3HF<sub>1</sub> mice, hepatomas and reticulum cell sarcomas (RCS), were affected by early thymectomy. Similarly, we observed no influence of 3 day thymic removal on the frequency of these two most commonly occurring neoplasms in C57BL strain mice: RCS=13% in seventy thymectomized mice and 10% in sixty-four intact mice; hepatomas=6% in thymectomized and 4% in intact mice—sexes combined. These findings confirm our earlier reports of lack of thymic influence on carcinogen-

induced hepatomas<sup>9</sup> and on RCS in SJL mice<sup>16</sup>. Mammary tumours were not observed in C57BL mice.

It was particularly interesting that more than a single primary neoplasm was found in many of the BC3HF<sub>1</sub> thymectomized mice (see footnotes, Table 1); it is difficult to relate this causally, however, to early thymectomy because of the small numbers. The striking influence of 3 day thymectomy on the frequency of late-occurring mammary tumours in which MTV is not a factor contrasts with earlier reports of the opposite effect: a reduced frequency and lengthened latent period on MTV-induced mammary tumours of C3H strain mice<sup>9,17,18</sup>.

A definitive immunological interpretation of the results of opposing influences of early thymectomy on MTV-induced versus non-viral mammary tumours is difficult to make at present. Two different antigenic components (TSTA) have been identified on mammary tumours which are immunogenic: one is cross-reactive and dependent on the MTV viral genome<sup>19,20</sup>; the other, also present on the tumour cell surface, lacks cross reactivity and seems not to be MTV-associated<sup>21,22</sup>. If immune deficits and TSTA are important factors in the induction and repression of both types of mammary tumours in the autochthonous host, one must assume that early thymectomy influences different components of the immune response in these two experimental situations. Work is in progress to test this possibility.

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- 1 Miller, J. F. A. P., Grant, G. A., and Roe, F. J. C., *Nature*, **199**, 920 (1963).
- 2 Trainin, J., Linker-Israeli, M., Small, M., and Borato-Chen, L., *Intern. J. Cancer*, **2**, 326 (1967).
- 3 Kirshstein, R. L., Rabson, A. S., and Peters, E. A., *Proc. Soc. Exp. Biol. Med.*, **117**, 198 (1964).
- 4 Defendi, V., and Roosa, R. A., in *The Thymus* (edit. by Defendi, V., and Metcalf, D.), 121 (The Wistar Institute Press, Philadelphia, 1964).
- 5 Allison, A. C., and Law, L. W., *Proc. Soc. Exp. Biol. Med.*, **127**, 207 (1968).
- 6 Law, L. W., *Cancer Res.*, **26**, 551 (1966).
- 7 Law, L. W., Ting, R. C., and Leckband, E., *Proc. US Nat. Acad. Sci.*, **57**, 1068 (1967).
- 8 Allison, A. C., and Taylor, R. B., *Cancer Res.*, **27**, 703 (1967).
- 9 Law, L. W., *Cancer Res.*, **29**, 1 (1969).
- 10 Metcalf, D., *Nature*, **208**, 1336 (1965).
- 11 Taylor, R. B., *Nature*, **208**, 1334 (1965).
- 12 Miller, J. F. A. P., *Nature*, **208**, 1337 (1965).
- 13 Crowle, H. J., and Hu, C. C., *Proc. Soc. Exp. Biol. Med.*, **127**, 190 (1968).



- <sup>14</sup> Heston, W. E., Deringer, M. B., and Dunn, T. B., *J. Nat. Cancer Inst.*, **16**, 1309 (1956).  
<sup>15</sup> Dunn, T. B., in *A Symposium in Mammary Tumours in Mice* (edit. by Moulten, F. R.), 13 (Amer. Assoc. Advance Sci. Publication No. 22, 1945).  
<sup>16</sup> McIntire, K. R., and Law, L. W., *J. Nat. Cancer Inst.*, **39**, 1197 (1967).  
<sup>17</sup> Martinez, C., *Nature*, **203**, 1188 (1964).  
<sup>18</sup> Law, L. W., *Nature*, **205**, 672 (1965).  
<sup>19</sup> Lavrin, D. H., Blair, P. B., and Weiss, D. W., *Cancer Res.*, **26**, 929 (1966).  
<sup>20</sup> Morton, D. L., *Proc. Amer. Assoc. Cancer Res.*, **5**, 46 (1964).  
<sup>21</sup> Morton, D. L., Miller, G. F., and Wood, D. A., *J. Nat. Cancer Inst.*, **42**, 290 (1969).  
<sup>22</sup> Vaage, J., *Nature*, **218**, 102 (1969).  
<sup>23</sup> Dunn, T. B., *J. Nat. Cancer Inst.*, **14**, 1281 (1954).

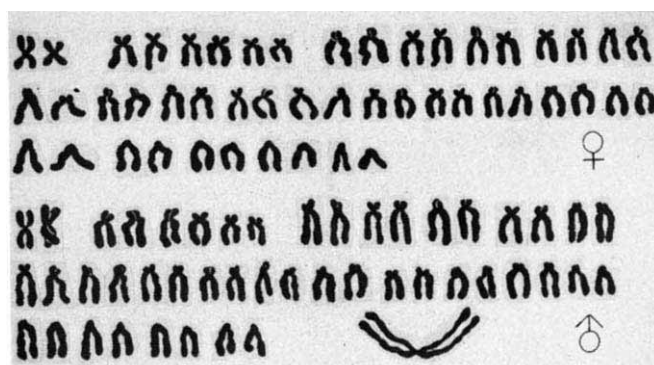


Fig. 1 Karyotype of the unnamed Mexican cyprinodontid fish.

## Multiple Sex Chromosomes in a Mexican Cyprinodontid Fish

THE chromosomes of the killifish<sup>1-3</sup> family Cyprinodontidae are being studied in many laboratories and the karyotypes of forty-eight of the approximately eighty-five species of North American killifishes have so far been determined (refs. 2 and 3 and our unpublished results), twenty-seven of them by us. All but three of the fifteen or sixteen North American genera of the family have been studied, and of the largest genera, *Fundulus* (twenty-nine species) and *Cyprinodon* (about twenty species), twenty-two and thirteen species, respectively, have been karyotyped. The diploid chromosome number of

This report concerns one species, representing an undescribed genus, which is unusual in that it has a diploid number of 48 in the female and 47 in the male. Chromosomes were prepared by the gill epithelium method of McPhail and Jones<sup>5</sup>. Fifty cells of three females and thirty-two cells of four males were examined. A testis squash was also made to give meiotic figures.

Somatic metaphase karyotypes of both sexes include one pair of metacentric, eighteen pairs of submetacentric-subtelocentric and four pairs of acrocentric chromosomes; in addition the female possesses a pair of acrocentric chromosomes and the male a single large metacentric chromosome (Figs. 1 and 2).

Table 1 Origin of the Mexican Cyprinodontid Karyotype

|        | Original state                         | Present state                                  | Gamete                            |
|--------|----------------------------------------|------------------------------------------------|-----------------------------------|
| Female | $2n=48:46 \text{ autosomes} + X_1 X_1$ | $2n=48:44 \text{ autosomes} + X_1 X_1 X_2 X_2$ | $22 + X_1 X_2$                    |
| Male   | $2n=48:46 \text{ autosomes} + X_1 Y$   | $2n=47:44 \text{ autosomes} + X_1 X_2 Y$       | $22 + X_1 X_2 \text{ or } 22 + Y$ |

American killifishes is usually 48. The known exceptions are species of the genus *Fundulus*<sup>3,4</sup> and *Lucania parva* (46), *L. interioris* (36) and *Adinia xenica* (32). The latter three species have large metacentric chromosomes indicating centric fusions; they can be enumerated by subtracting the total number of chromosomes from 48. For example, *Adinia* has sixteen large metacentrics, the thirty-two chromosomes being subtracted from 48.

The unpaired chromosome in the male is about three to five times longer than any other chromosome.

Heterogamety has been observed only recently in fishes. In their summary of this subject, Ebeling and Chen<sup>6,7</sup> mentioned  $XX-XY$  and  $XX-XO$  types in about twenty species of the 200 that have been karyotyped; of these, twelve are from the specialized deep sea habitat. Ours is the first example of a multiple sex chromosome mechanism in fishes. The occurrence

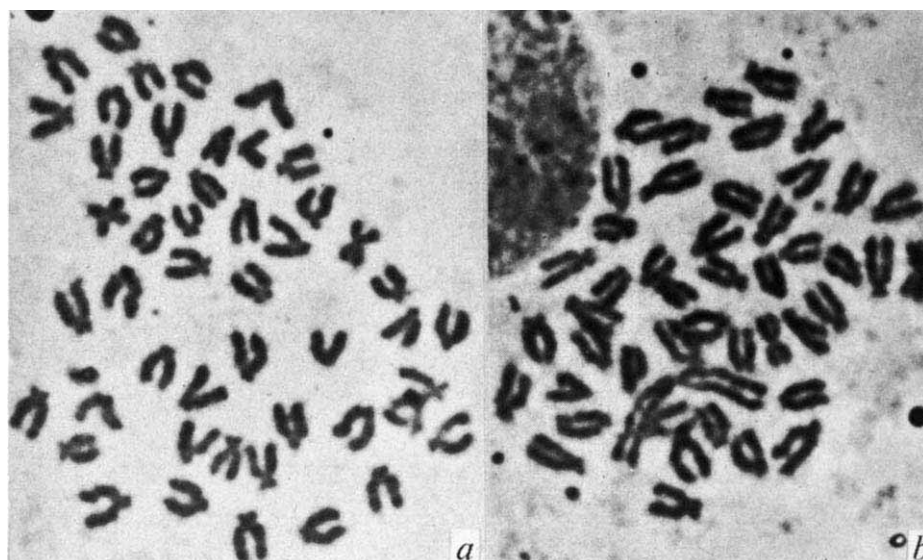
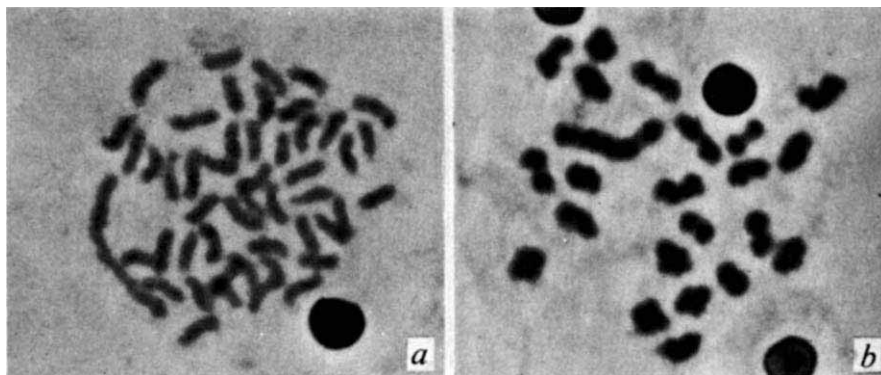


Fig. 2 Photomicrographs of somatic chromosome complements of female (a) ( $2n=48$ ) and male (b) ( $2n=47$ ) of the cyprinodontid ( $\times 1,900$ ).

Fig. 3 *a*, Spermatogonial prophase; note the long Y chromosome at left, *b* Diakinesis in meiosis ( $\times 2,850$ ).



of multiple sex chromosomes in the animal kingdom has been reviewed with an extensive bibliography<sup>8,9</sup>. The  $X_1X_1X_2X_2-X_1X_2Y$  type has been found recently in lizards of the genus *Anolis*<sup>10</sup> and in a rodent, *Mus minutoides*<sup>11</sup>.

The most reasonable explanation for the karyotype of this seemingly unique fish is that the female has forty-four autosomes and  $X_1X_1X_2X_2$  acrocentric sex chromosomes, whereas the male has forty-four autosomes and  $X_1X_2$  acrocentric sex chromosomes plus a Y chromosome that is the largest of the metacentric chromosomes. We think that the explanation for the origin of the multiple sex chromosomes in this fish is similar to that suggested by Matthey<sup>11</sup> for *Mus minutoides*, namely that one autosome has fused with the primitive Y chromosome.

The ancestor of the Mexican fish probably had a diploid number of forty-eight, as in the thirteen species of *Cyprinodon* studied so far. That the new genus is most closely related to *Cyprinodon* is suggested by the many shared morphological characters, for example, tricuspid teeth, body shape, size, position, number of fin rays and squamation<sup>12,13</sup>. At some stage in evolution, both sexes had morphologically identical karyotypes that included forty-six autosomes and indistinguishable sex chromosomes, X and Y. Subsequently the Y chromosome in the male fused with an acrocentric autosome morphologically indistinguishable from the sex chromosomes. By definition the homologue of the fused autosome in the male and the corresponding autosome pair in the female now become an additional X chromosome,  $X_2$ . Table 1 summarizes this situation.

The Y chromosome of the Mexican killifish differs from that of other animals with multiple sex chromosomes in being considerably longer than the combined length of any two acrocentric chromosomes, two of which are supposed to be the  $X_1$  and  $X_2$  chromosomes. This means that the Y chromosome probably originated not only by a Robertsonian fusion of acrocentric chromosomes—the male has one less acrocentric chromosome than the female—but also by some addition of chromatin.

In the testis squash, the long Y chromosome is clear at the spermatogonial prophase (Fig. 3a); at diakinesis (Fig. 3b) there are twenty-two bivalents and one trivalent in which  $X_1X_2$  seems to be attached to both ends of Y as a trivalent.

The discovery of multiple sex chromosomes in fishes strengthens the belief that the cytological sex-determining mechanism includes a more complex pattern than was previously thought to characterize these vertebrates<sup>11</sup>. Additional studies of fish chromosomes may reveal a diversity in this mechanism, as in higher vertebrates.

We thank H. Gay, D. M. Lay, J. B. Burch, C. M. Patterson and Clark Hubbs for advice. This work was supported by the US National Science Foundation.

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- <sup>1</sup> Scheel, J., *Rivulins of the Old World* (TFH Publications, New Jersey, 1968).
- <sup>2</sup> Chen, T. R., and Ruddle, F. H., *Chromosoma*, **29**, 255 (1969).
- <sup>3</sup> Setzer, P. V., *Trans. Amer. Fish. Soc.*, **99**, 139 (1970).
- <sup>4</sup> Chen, T. R., *Chromosoma* (in the press).
- <sup>5</sup> McPhail, J. D., and Jones, R. L., *J. Fish. Res. Board Canada*, **23**, 767 (1966).
- <sup>6</sup> Ebeling, A. W., and Chen, T. R., *Trans. Amer. Fish. Soc.*, **99**, 131 (1970).
- <sup>7</sup> Chen, T. R., *Postilla* (Yale Univ.), 130 (1969).
- <sup>8</sup> White, M. J. D., *Animal Cytology and Evolution*, second ed. (Cambridge University Press, 1954).
- <sup>9</sup> Mittwoch, U., *Sex Chromosomes* (Academic Press, New York, 1967).
- <sup>10</sup> Gorman, G. C., and Atkins, L., *Amer. Nat.*, **100**, 579 (1967).
- <sup>11</sup> Matthey, R., *Chromosoma*, **16**, 35 (1965).
- <sup>12</sup> Miller, R. R., *Misc. Publ. Mus. Zool. Univ. Mich.*, **68** (1948).
- <sup>13</sup> Miller, R. R., *Occ. Pap. Mus. Zool. Univ. Mich.*, **581** (1956).

## Antagonistic Effects of Alpha and Beta-adrenergically Coded Hypothalamic Neurones on Consummatory Behaviour in the Rat

In the past 5 years, we have demonstrated the diametrically opposite effects of alpha-adrenergic and beta-adrenergic amines on water balance in the albino rat. Isoproterenol, a beta-adrenergic agonist, when injected subcutaneously in single doses of 0.05–5.25 mg/kg body weight, produced in animals sated with water a copious drinking and simultaneous inhibition of the urine flow lasting about 3 h. In contrast with this paradoxical phenomenon, the administration of metaraminol, an alpha-adrenergic agonist, induced a water depleting reaction. Rats subcutaneously injected with 0.63–10.0 mg/kg body weight of metaraminol excreted large volumes of dilute urine but made no immediate efforts towards recouping this massive water loss by drinking. Both the water depleting and water sparing response could be obviated readily by treating the rats with equimolecular quantities of either alpha or beta-adrenergic blocking agents before administration of the respective agonist. These findings seemed to be consistent with the existence of central nervous system circuits of water regulation which are chemically coded to respond in antagonistic fashion to selective alpha or beta-adrenergic stimulation<sup>1</sup>.

In the light of these observations on water balance and the importance of several adrenergic amines as anorexic agents, it seemed interesting to look for a similar pattern of contrasting effects of alpha and beta-adrenergic stimulation in the central regulation of food intake.

It had already been established that direct application of norepinephrine to the lateral hypothalamus<sup>2</sup> and to the



perifornical region<sup>3</sup> produces eating in food sated albino rats and that pretreatment with the alpha-adrenergic blocking agent, phentolamine, inhibited this food consumption. Further, animals treated with noradrenaline not only ate voraciously, but also stopped drinking<sup>4</sup>. This report deals with the effects of a series of biogenic amines on eating behaviour following subcutaneous<sup>5</sup> and direct intracranial administration in a further attempt to elucidate the opposing influences exerted by alpha and beta-adrenergically coded neurones.

In the experiments with subcutaneous injections, groups of ten adult male albino rats of the Sprague-Dawley strain were allowed access to Purina Chow for only 3 h each day. After a stable baseline had been established on this feeding schedule, drugs were administered 5 min before the 3 h feeding period. Autonomic blocking agents were given 15 min before the agonists.

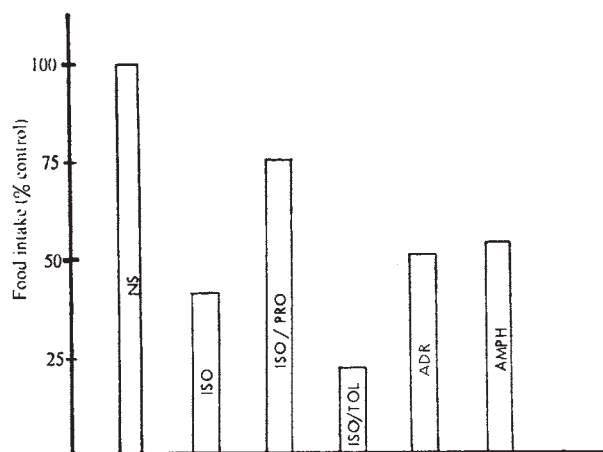


Fig. 1 Effect of isoproterenol, administered by the subcutaneous route, on food consumption in the food-deprived rat. ISO, Isoproterenol HCl (0.1 mg/kg); NS, normal saline control; PRO, propranolol HCl (6.0 mg/kg beta-antagonist); TOL, tolazoline (8.5 mg/kg alpha-antagonist); ADR, adrenaline bitartrate (0.5 mg/kg); AMPH, amphetamine (0.5 mg/kg). Each group consisted of a minimum of ten animals. Analysis of *P* values showed all results significant beyond *P* < 0.01.

Fig. 1 shows the effects of several representative agents on food intake. The subcutaneous injection of small amounts of dl-isoproterenol HCl (0.1 mg/kg body weight) caused a marked reduction in food intake, following 21 h of food deprivation. Whereas control animals ate 6.5 g in the first hour, isoproterenol treated rats consumed less than 2.0 g during this interval (60% inhibition). The anorexic effects of isoproterenol could be significantly inhibited when propranolol (beta-adrenergic antagonist) was injected 15 min before isoproterenol. On the other hand, pretreatment with an alpha-adrenergic blocking agent (tolazoline) enhanced the isoproterenol inhibition (facilitation of beta-adrenergic preponderance) as evidenced by a further reduction of food intake to only 18% of control value (82% inhibition). When isoproterenol was compared with d-amphetamine (by subcutaneous injection) for anorexic potential, it was found to be four to five times more effective than the latter on a weight basis. This method of selective adrenergic blockade thus served to uncover the apparent existence of counter balanced antagonistic alpha and beta-adrenergic influences in the central regulation of feeding behaviour<sup>5</sup>. Leibowitz<sup>6</sup> has provided direct experimental evidence for the validity of our hypothesis by demonstrating that similar effects can be elicited by application of beta-adrenergic agonists and blocking agents to the brain.

In our experiments using direct intracranial chemical stimulation, 50 Sprague-Dawley male albino rats were stereotactically

implanted, under 'Avertin' anaesthesia, with stainless steel cannula systems for the injection of microlitre quantities of aqueous solutions of various amines. The cannulas were placed in the perifornical hypothalamus in all cases. After 1 week for recovery, the animals were fasted for 21 h and observed for eating and drinking patterns until their 3 h food and water consumption had stabilized. The rats were then used in a simple cross-over design with each rat acting as its own control. At no time was a volume greater than 2.0 µl. injected intracranially.

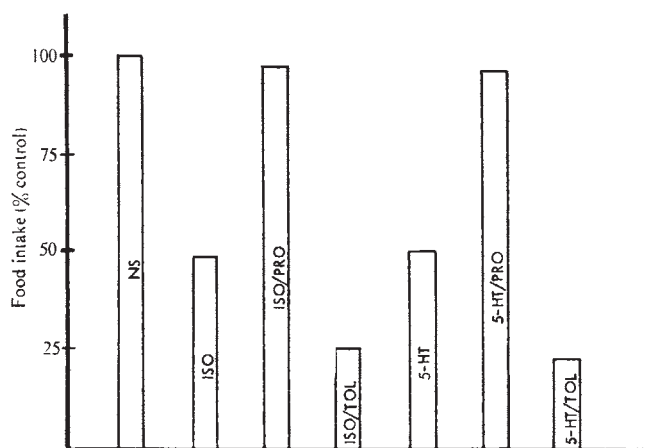


Fig. 2 Effect of isoproterenol, administered by the intrahypothalamic route, on food consumption in the food-deprived rat. NS, Normal saline control; ISO, isoproterenol (37.0 µg); PRO, propranolol (44 µg); TOL, tolazoline (20 µg); 5-HT, serotonin (18 µg). Each group consisted of a minimum of ten animals. Analysis of *P* values showed all data significant beyond *P* < 0.01.

Fig. 2 shows the effects of isoproterenol application alone and after selective alpha or beta-adrenergic blockade. These findings are qualitatively and quantitatively similar to those seen with the subcutaneous injections of isoproterenol, which in a dose of 30 µg/rat, produced a 65% decrease in food intake. This effect was reversed by propranolol and enhanced by the alpha-adrenergic antagonist, tolazoline. Each of the animals used in our studies also responded positively to norepinephrine treatment by eating when sated.

Serotonin inhibited eating in a manner similar to isoproterenol, thus extending earlier observations on drinking. We had previously confirmed the finding that the subcutaneous injection of serotonin produced copious drinking in the rat<sup>7</sup> and had demonstrated that this effect could be antagonized selectively by beta-adrenergic blockade with propranolol<sup>8</sup>. When serotonin was administered either by subcutaneous injection or intracranially to the perifornical hypothalamus, it proved a potent anorexic agent the effect of which could be blocked by propranolol. Thus, serotonin again displayed beta-adrenergic properties when applied to the adrenergic feeding system. This finding may have important implications for the role of the neurones containing serotonin which are densely concentrated within the hypothalamus.

The data presented here substantiate our earlier proposal<sup>5,9</sup> that circuits subserving consummatory behaviour in the rat are chemically coded to respond to both alpha and beta-adrenergic stimulation and further that selective activation of either alpha or beta-adrenergic neurones evokes diametrically opposite effects.

This work was supported by grants from the National Institutes of Health, US Public Health Service, and the Hoffman-LaRoche Foundation. There has been a generous interchange of information between this laboratory and Dr Neal Miller's Department at Rockefeller University, with Dr Leibowitz

advising on brain cannulation procedures in our work, and one of us (H. W. G.) aiding with the pharmacological interpretation of her findings.

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- <sup>1</sup> Lehr, D., Mallow, J., and Krukowski, M., *J. Pharmacol. Exp. Therap.*, **158**, 150 (1967).
- <sup>2</sup> Grossman, S. P., *Science*, **132**, 301 (1960).
- <sup>3</sup> Leibowitz, S. F., and Miller, N. E., *Science*, **165**, 609 (1969).
- <sup>4</sup> Grossman, S. P., *Amer. J. Physiol.*, **202**, 1230 (1962).
- <sup>5</sup> Conte, M., Lehr, D., Goldman, W., and Krukowski, M., *Pharmacologist*, **10**, 180 (1968).
- <sup>6</sup> Leibowitz, S. F., *Nature*, **226**, 963 (1970).
- <sup>7</sup> Zamboni, P., *Boll. Soc. Ital. Biol.*, **42**, 1657 (1967).
- <sup>8</sup> Goldman, W., and Lehr, D., *Pharmacologist*, **9**, 249 (1967).
- <sup>9</sup> Lehr, D., Mallow, J., Krukowski, M., and Colon, R., *Fed. Proc.*, **25**, 624 (1966).

## Enzyme Variants as Markers in the Study of Pre-copulatory Isolating Mechanisms

REPRODUCTIVE isolation is the basic process in the speciation of outbreeding sexual organisms<sup>1,2</sup>, and populations can become reproductively isolated by intrinsic, heritable mechanisms operating before or after copulation. The post-copulatory mechanisms, typically represented by hybrid sterility, can be tested by crossing experiments, but it is much more difficult to demonstrate pre-copulatory barriers to gene flow.

In most cases pre-copulatory isolating mechanisms between two allopatric forms can be studied reliably only by release experiments, a crucial requirement being the availability of good natural markers to distinguish the two forms and their hybrids. At the lower stages of evolutionary divergence, conventional morphology rarely provides discriminant characters, but enzyme variants may be useful. In fact, populations or population samples characterized by different allozymes seem to be frequently available and their use may avoid lengthy breeding and selection procedures which are likely to influence the behavioural characters involved in reproductive isolation. This is especially true for the selection of recessive morphological mutants which have been found in many cases to differ strongly from the wild type in mating propensity<sup>3</sup>. Here we report the use of enzyme variants in the study of pre-copulatory isolating mechanisms between two members of the *mariae* complex of the genus *Aedes* (Diptera, Culicidae).

The *mariae* complex includes at least three forms (*mariae*, *zammitii* and *phoeniciae*) apparently allopatric, slightly differentiated morphologically and showing various degrees of hybrid sterility<sup>4,5</sup>. The larvae of these mosquitoes have an apparently identical adaptation to breeding in rock pools along the Mediterranean coasts. In optimal conditions the egg-adult cycle may be completed in less than 10 days and the minimum duration of one generation is less than 15 days. The distribution is western Mediterranean for *mariae* and eastern Mediterranean for *zammitii* and *phoeniciae*. The latter has been recorded from Cyprus and from the coasts of Israel, Lebanon and Syria while *zammitii* occurs on the Adriatic, Ionian and Aegean coasts. The zones where such ranges of distribution

may come in contact, eventually overlapping, were fully investigated in the case of Sicily, where *mariae* and *zammitii*, although separated only by stretches of sandy coasts, were never found to coexist in one locality.

A complete sterility barrier was demonstrated between *phoeniciae* and the other two members of the complex and, accordingly, this sibling has been proposed as a valid species. Hybrid sterility also occurs between *mariae* and *zammitii* but the F<sub>1</sub> hybrid males are only partially sterile in this cross while the F<sub>1</sub> hybrid females are fertile. On the other hand, no pre-copulatory barrier to gene flow was revealed by cage experiments so that, considering the laboratory evidence for introgressive hybridization and the lack of data on reproductive isolation in nature, the taxonomic status of *mariae* and *zammitii* remained uncertain. The morphological differences between *zammitii* and *mariae* are sufficient to identify allopatric populations biometrically but do not permit a reliable identification of single individuals in cases where the possibility of occasional hybrids must be taken into consideration. For the cytotoxic approach this gave negative results, for no favourable polytene chromosomes are available in these mosquitoes.

The study of reproductive isolation of *mariae* and *zammitii* in nature was made possible by a release experiment on populations of *mariae* from Sperlonga (on the Tyrrhenian coast) and of *zammitii* from Peschici (on the Adriatic coast). These populations were previously found to be monomorphic for distinct PGM electrophoretic patterns showing a simple Mendelian inheritance<sup>6</sup>. Assuming two codominant alleles, Pgm<sup>A</sup> and Pgm<sup>B</sup>, the Peschici and Sperlonga populations appeared as homozygous Pgm<sup>A</sup>/Pgm<sup>A</sup> and Pgm<sup>B</sup>/Pgm<sup>B</sup> respectively while the hybrids were heterozygotes Pgm<sup>A</sup>/Pgm<sup>B</sup>. Accordingly the three corresponding PGM patterns were utilized to identify *zammitii*, *mariae* and their hybrids in the release zone.

About 25,000 larvae and pupae of *zammitii* were collected at Peschici and released at Sperlonga (Torre Capovento) on July 14, 1970. The release zone covers less than 1 km of rocky coast between two sand beaches and the *mariae* breeding places, during the breeding season, generally comprise no more than eighteen rock pools. The density of *mariae* in this locality had been previously lowered, more than 20,000 larvae and pupae having been collected and destroyed during June and July. The number of *zammitii* released was calculated to approach the number of *mariae* present, taking into account the existence in the zone of adult females of *mariae* and of eggs which can remain quiescent for long periods in these mosquitoes. Fourth instar larvae and pupae were sampled on July 15, 19, 22 and 26 and weekly from July 26 to October 11. Samples were taken from all positive breeding places, the number of specimens collected never exceeding 10% of those present. The material was brought to the laboratory and the adults emerging were identified according to their PGM pattern. The results summarized in Table 1 show the almost complete absence of hybrids in all the samples. The ratio *zammitii* to *mariae* was nearly 1 : 1 during most of August. Subsequently the two forms predominated alternately, suggesting an ecotypic divergence presumably involving oviposition behaviour or egg hatching.

Vigorous adult hybrids are obtained in the laboratory in the expected number, so the only explanation of their extreme rarity in nature is the existence of efficient pre-copulatory isolating mechanisms between *zammitii* and *mariae*. The lack of introgressive hybridization was also indicated by the constancy of some biometric difference previously described<sup>3</sup> and known to be polygenic (M. C., unpublished). On this evidence, *mariae* and *zammitii* are to be regarded as sibling species.

The actual distribution pattern of *mariae* and *zammitii* suggests a process of speciation originated from a disjunction of a primitive circum-Mediterranean range of distribution. Assuming such a process of speciation as truly allopatric the pre-copulatory barrier existing between these siblings seems to



be a by-product of the genetic divergence. On the other hand, the incompleteness of hybrid sterility shown by the crossing experiments contrasts with the high efficiency of the pre-copulatory mechanisms of isolation suggesting that the latter were the first to develop in this case.

**Table 1** Absolute Frequencies of PGM Phenotypes in Samples collected at Different Times after the Release Date (July 14, 1970)

| Date         | PGM phenotypes |    |     | Total tested |
|--------------|----------------|----|-----|--------------|
|              | A              | AB | B   |              |
| July 15      | 166            | —  | 48  | 214          |
| July 19      | 103            | —  | 9   | 112          |
| July 22      | 105            | —  | 18  | 123          |
| July 26      | 112            | 1  | 32  | 145          |
| August 2     | 93             | 3  | 70  | 166          |
| August 9     | 60             | —  | 77  | 137          |
| August 16    | 155            | 1  | 144 | 300          |
| August 23    | 55             | —  | 62  | 117          |
| August 30    | 235            | 2  | 87  | 324          |
| September 6  | 29             | —  | 166 | 195          |
| September 13 | 27             | —  | 180 | 207          |
| September 20 | 112            | 1  | 56  | 169          |
| September 27 | 118            | 2  | 64  | 184          |
| October 4    | 42             | —  | 89  | 131          |
| October 11   | 2              | —  | 10  | 12*          |

\* The number of mosquitoes tested on October 11 is very low because the sample was collected after the hibernation period had begun.

Our experiment clearly shows the value of enzyme variants in the study of pre-copulatory isolating mechanisms and the importance of this approach seems relevant not only to evolutionary genetics but also to the planning of genetic control measures against insect pests.

This work was supported by grants from the Italian Ministry of Health and from the Italian Research Council (Centro di Studio per la Genetica Evoluzionistica).

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Received October 22; revised December 26, 1970.

<sup>1</sup> Dobzhansky, T., *Genetics and the Origin of Species* (Columbia University Press, New York, 1951).

<sup>2</sup> Mayr, E., *Animal Species and Evolution* (Harvard University Press, Cambridge, 1963).

<sup>3</sup> Spiess, E. B., in *Essays in Evolution and Genetics in Honor of T. Dobzhansky* (North-Holland, Amsterdam, 1970).

<sup>4</sup> Coluzzi, M., and Sabatini, A., *Riv. Parassit.*, **29**, 49 (1968).

<sup>5</sup> Coluzzi, M., Gironi, A. M., and Muir, D. A., *Parassitologia*, **12**, 119 (1970).

<sup>6</sup> Coluzzi, M., Bullini, L., and Bianchi Bullini, A. P., *Biochem. Genet.* (in the press).

## Increased Fertility in Males with the Sick Cell Trait?

At least two mechanisms have been proposed to account for the maintenance of high frequencies of the haemoglobin S gene in areas of endemic malaria: differential mortality (operating primarily on children)<sup>1-5</sup> and increased fertility among A/S females<sup>6-8</sup>.

Childhood mortality has been thought to be the principal factor in continuing selection for the S gene<sup>2-5</sup>. Several

authors, however<sup>9-11</sup>, have pointed out extensive discrepancies between the number of A/A children who should die (to proportionately reduce the adult A frequency and maintain it constant with regard to the S frequency) and the number who actually do. Further, we are aware of no extensive studies in which the age related decrease in the frequency of A/A individuals is sufficient to support a stable frequency of the S gene. In many reports there is little change in the ratio between numbers of A/S and A/A children in progressively older age groups<sup>6,12</sup>.

A second mechanism, that of increased fertility on the part of the A/S female, has been proposed and partially substantiated<sup>6-8</sup>. It has been suggested that fewer A/S females suffer placental infection during pregnancy, so that there are more live births<sup>7</sup>. We propose that enhanced fertility of the A/S male may be a third mechanism maintaining the S gene in high frequency in malarious areas.

MacLeod and Hotchkiss<sup>13</sup> have shown that artificial elevation of the scrotal temperature of the adult male above 37° C (it is normally about 35° C) for 45 min may cause azoospermia followed by a recovery period of reduced sperm count which may last more than 2 months. In fact, Amelar<sup>14</sup> suggests that simply elevating scrotal temperature to that of the body may result in azoospermia. Mills<sup>15</sup>, MacLeod<sup>16</sup> and others have associated fevers accompanying disease states such as chickenpox and pneumonia with depression of both the number and the motility of sperm.

Fever peaks which accompany malarial attack may frequently exceed 40° C<sup>17</sup> and may last for 8 h or longer<sup>18</sup>. Studies previously cited indicate that febrile episodes such as these should be sufficient to significantly depress male fertility for a period of 1-2 months. One investigation conducted in a hyperendemic region indicates that malarial attacks strike the average adult about twice a year<sup>17</sup>. In a hyperendemic area, therefore, the fertility of less resistant males may be depressed for a total of 2-4 months/yr.

Most of the work comparing infection rates and parasite counts in A/A and A/S individuals has been restricted to children below the age of 10, and the data available on adults are scanty. Allison<sup>5</sup>, however, found that immune adult A/S males were much less likely to develop malaria when inoculated intravenously with *P. falciparum*. The studies of Buetler *et al.*<sup>19</sup> were less conclusive, but indicated that adult A/S males had lower parasite counts and developed them more slowly after inoculation. Even slight differences in peak parasitaemia between A/A and A/S adult males should be important, because it has been shown that the numbers of parasites which may precipitate febrile episodes are much lower for adults than for children<sup>17</sup>.

There is some evidence to support the importance of A/S in the maintenance of male fertility. Roberts and Boyo<sup>20</sup> and Allison<sup>21</sup> found that A/S × A/A marriages, regardless of the sex of the sickling parent, produced more live births per fertile year of marriage than did A/A × A/A marriages. Further, Allard<sup>12</sup> reports significantly higher fertility among A/S males in the Belgian Congo. We feel that the data showing (1) a definite decline in fertility following febrile episodes, (2) the rather frequent occurrence of paroxysms in most members of "immune" populations in hyperendemic areas and (3) the probability that A/S males are likely to experience lower and more short lived fevers indicate that an increased fertility of the A/S male probably contributes to the maintenance of high frequencies of the S gene in malarious areas.

We thank Professor Frank B. Livingstone for advice and criticism.

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- <sup>1</sup> Garlick, J. P., *Trans. Roy. Soc. Trop. Med. Hyg.*, **54**, 146 (1960).
- <sup>2</sup> Motulsky, A. G., Vandepitte, J., and Fraser, G. R., *Amer. J. Human Genet.*, **18**, 514 (1966).
- <sup>3</sup> Raper, A. B., *Brit. Med. J.*, **1**, 1186 (1955).
- <sup>4</sup> Raper, A. B., *Trans. Roy. Soc. Trop. Med. Hyg.*, **53**, 110 (1959).
- <sup>5</sup> Allison, A. C., *Brit. Med. J.*, **1**, 290 (1954).
- <sup>6</sup> Delbrouck, J., *Ann. Soc. Belge Med. Trop.*, **38**, 103 (1958).
- <sup>7</sup> Livingstone, F. B., *Brit. Med. J.*, **1**, 762 (1957).
- <sup>8</sup> Firschein, L. I., *Amer. J. Human Genet.*, **13**, 233 (1961).
- <sup>9</sup> Foy, H., Brass, W., Moore, R. A., Timms, G. L., Kondi, A., and Oluoch, T., *Brit. Med. J.*, **2**, 1116 (1955).
- <sup>10</sup> Raper, A. B., *Brit. Med. J.*, **1**, 965 (1956).
- <sup>11</sup> Rucknagel, D. L., and Neel, J. V., *Progress in Human Genetics* (edit. by Steinberg, A.) (1961).
- <sup>12</sup> Allard, R., *Ann. Soc. Belge Med. Trop.*, **35**, 649 (1955).
- <sup>13</sup> MacLeod, J., and Hotchkiss, R. S., *Endocrinology*, **28**, 780 (1941).
- <sup>14</sup> Amelar, R. D., *Infertility in Men* (Davis, Philadelphia, 1966).
- <sup>15</sup> Mills, R. G., *J. Exp. Med.*, **30**, 505 (1919).
- <sup>16</sup> MacLeod, J., *Fertil. Steril.*, **2**, 523 (1951).
- <sup>17</sup> Miller, M., *Trans. Roy. Soc. Trop. Med. Hyg.*, **52**, 152 (1958).
- <sup>18</sup> Russel, P. F., West, L. F., and Manwell, R. D., *Practical Malariaology* (Oxford University Press, London, 1963).
- <sup>19</sup> Buetler, E., Dern, R. J., and Flanagan, C. L., *Brit. Med. J.*, **1**, 1189 (1955).
- <sup>20</sup> Roberts, D. F., and Boyo, A. E., *Ann. Human Genet.*, **24**, 375 (1960).
- <sup>21</sup> Allison, A. C., *Ann. Human Genet.*, **21**, 67 (1956).

## Ethnic Differences in Human Blood Cell Sodium Concentration

BALFE *et al.*<sup>1</sup> have described a Negro family whose red blood cells had a high sodium concentration. The mean red cell sodium concentration in eight members of the family studied was 14.4 mmol l.<sup>-1</sup> of cells, compared with 7.6 mmol l.<sup>-1</sup> of cells in controls. Our studies of sodium and potassium concentrations in the blood cells of patients with hypertension have suggested that red cell sodium concentration is frequently greater in Negro than in Caucasian subjects.

The methods of estimating blood cell ion concentrations and water content have been described already<sup>2,3</sup>. Freshly drawn blood was centrifuged in standardized conditions and the sodium, potassium and water content of weighed samples of plasma and of the packed cell column were measured. Corrections were applied to the measured cell contents to allow for plasma trapped in the packed cell column. The centrifugal conditions used differed from those used previously. Five 3.5 g aliquots of heparinized blood (three for cation concentration and two for water content) were spun for 15 min at 11,000 r.p.m. in a swing-out head on an MSE Highspeed 18 at 10° C. (RCF at the base of the tubes was 15,000g.) These centrifugal conditions result in the inclusion of white as well as red cells in the packed cell column and a different regression equation must be used for estimating plasma trapping, derived from experiments in which <sup>24</sup>NaCl was added to 105 blood samples from eleven healthy subjects. Blood samples were then immediately centrifuged in the manner described and the percentage of <sup>24</sup>Na trapped in the packed cell column ( $x$ ) related to the weight in grams of cells sampled ( $y$ ). In these centrifugal conditions  $x = 2.182 + 0.112 y$ .

Blood cells from 142 Caucasian and thirty-three Negro subjects, the latter all born in West Africa or the West Indies, were studied. The median water, sodium and potassium contents per kg of cells for Caucasian and Negro subjects, together with the Mann-Whitney U statistic<sup>4</sup> and one-tailed  $P$  are listed for each of five subgroups in Table 1. The results for men and women were examined separately, as differences attributable to sex have been reported<sup>2</sup>. The healthy men were not hospital outpatients. No healthy women were studied. Hypertensive subjects included patients with renal and essential hypertension, but excluded patients with sus-

pected or proven endocrine disease; they were divided into those receiving, and those not receiving, treatment with diuretic drugs of the thiazide type. No significant differences were found as a result of treatment with other types of anti-hypertensive drug. For the women, median age in years is also listed, as both the water and sodium contents of blood cells change with age in women (but not in men)<sup>2</sup>. Blood cells were examined on a number of occasions in many subjects; for these subjects mean values were used for analysis.

**Table 1** Comparison of Water, Sodium and Potassium Contents of Blood Cells of Caucasian and Negro Subjects

| Subgroup                                               |                  | Cau-<br>sian | Negro | Mann-<br>Whitney<br>U | One-<br>tailed<br>P |
|--------------------------------------------------------|------------------|--------------|-------|-----------------------|---------------------|
| Healthy men                                            | <i>n</i>         | 37           | 9     |                       |                     |
|                                                        | H <sub>2</sub> O | 637.4        | 637.2 | 153                   | NS                  |
|                                                        | Na               | 7.245        | 9.046 | 27                    | 0.00007             |
|                                                        | K                | 88.11        | 86.59 | 90                    | 0.017               |
| Hypertensive men<br>not treated                        | <i>n</i>         | 38           | 7     |                       |                     |
|                                                        | H <sub>2</sub> O | 631.3        | 627.7 | 111                   | NS                  |
|                                                        | Na               | 7.730        | 9.032 | 69.5                  | 0.023               |
|                                                        | K                | 88.78        | 87.98 | 96                    | NS                  |
| Hypertensive men<br>treated with<br>diuretics          | <i>n</i>         | 20           | 5     |                       |                     |
|                                                        | H <sub>2</sub> O | 638.4        | 628.4 | 49                    | NS                  |
|                                                        | Na               | 7.864        | 12.11 | 14                    | <0.025              |
|                                                        | K                | 88.84        | 86.44 | 23                    | <0.05               |
| Hypertensive<br>women not<br>treated with<br>diuretics | <i>n</i>         | 29           | 8     |                       |                     |
|                                                        | Age              | 53           | 40    |                       |                     |
|                                                        | H <sub>2</sub> O | 631.9        | 644.6 | 60                    | 0.019               |
|                                                        | Na               | 7.444        | 9.478 | 39                    | 0.0023              |
| Hypertensive<br>women treated<br>with diuretics        | <i>n</i>         | 18           | 4     |                       |                     |
|                                                        | Age              | 53           | 43    |                       |                     |
|                                                        | H <sub>2</sub> O | 636.0        | 634.1 | 34                    | NS                  |
|                                                        | Na               | 7.535        | 9.960 | 5                     | <0.01               |
|                                                        | K                | 90.97        | 88.06 | 14.5                  | <0.05               |

For each subgroup are listed the number of subjects ( $n$ ), median blood cell water content (g kg<sup>-1</sup>), and median blood cell sodium and potassium contents (mmol kg<sup>-1</sup>). For women median age in years is also listed.

In all five subgroups, the blood cell sodium concentration was significantly greater in Negro than in Caucasian subjects. Red cell sodium concentration increases with age in women<sup>2</sup>. The Negro women studied, although on average more than 10 yr younger than their Caucasian counterparts, had greater cell sodium concentrations.

In all five subgroups the blood cell potassium concentration was greater in Caucasian than in Negro subjects. The absence of, or lesser statistical significance of, the differences in potassium concentration may in part be attributable to the negative correlation between the potassium and haemoglobin contents of cells<sup>2</sup>. Many of the subjects studied were women, or men attending hospital, in whom greater variations of cell haemoglobin content might be anticipated than among healthy volunteers. In the healthy men studied, the difference in cell potassium concentration was statistically significant.

Only in the group of hypertensive women not receiving treatment with thiazide diuretics were there significant differences in cell water content. In healthy women, the red cell water content has been found to increase slightly with increasing age<sup>2</sup>. The Negro women of this subgroup, although younger than the Caucasian women, had a greater cell water content. This finding may also be related to a lower haemoglobin content of the cells.



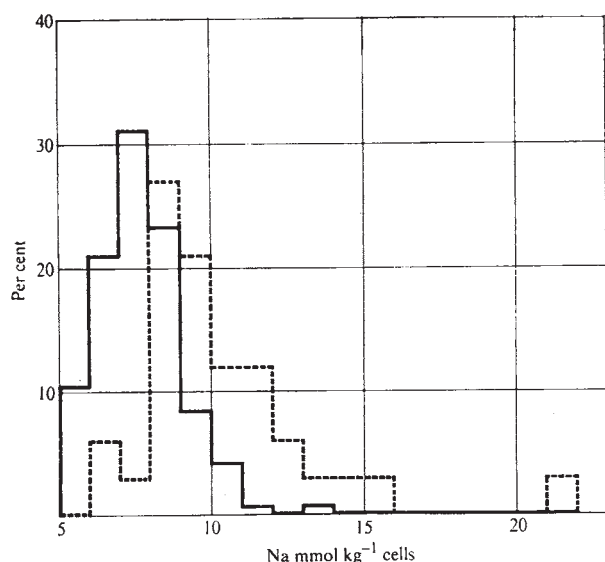


Fig. 1 Percentage of Caucasian subjects (continuous line) and of Negro subjects (interrupted line) with blood cell Na concentration at each 1 mmol increment from 5 to 22 mmol kg<sup>-1</sup> of cell.

The ratio of Negro to Caucasian subjects in the five subgroups did not vary greatly (0.243, 0.189, 0.250, 0.276 and 0.222 respectively) and because of this, and the very small numbers in each, the subgroups have been pooled to produce a frequency distribution of blood cell sodium concentration (Fig. 1).

A haemoglobin variant was found in three of the eleven Negro patients in whom this was sought. Two were heterozygous for haemoglobin S (12.25 and 6.60 mmol Na kg<sup>-1</sup> of cells) and one for haemoglobin C (9.98 mmol Na kg<sup>-1</sup> of cells); the median red cell sodium concentrations for the eight subjects homozygous for haemoglobin A, which included the patient with the greatest concentration of all, was 10.22 mmol kg<sup>-1</sup> of cells. Although the numbers are very small, there is no evidence of an association between red cell sodium concentration and particular haemoglobin variants.

Two factors, neither of which we studied, may be in part responsible for these ethnic differences. Brewer<sup>5</sup> found that mean red cell adenosine triphosphate (ATP) concentration in Negroes was less than in Caucasians (3.17 and 3.47  $\mu\text{mol g}^{-1}$  of haemoglobin, respectively), and Balfe *et al.*<sup>1</sup> in their study of eight members of a Negro family (with a mean red cell sodium concentration 14.4 mmol l.<sup>-1</sup> of cells) found that ouabaine-sensitive sodium efflux averaged 49.7%, and ouabaine-sensitive ATPase activity 50.6%, that of control cells, the source of the control cells not being specified. Measurements of the number of ouabaine-binding sites per cell, analogous to those carried out with sheep cells<sup>6</sup>, have not been made on human cells from Caucasian and Negro subjects. Thus it is possible that the greater concentration of sodium, and lesser concentration of potassium, found in the blood cells of Negro than of Caucasian subjects is attributable to some difference in the availability or steady-state activity of membrane Na-K ATPase in the two groups.

We thank Mrs Ruth Mason for technical assistance, Mr D. Field for help in computing the results, Professor H. Harris for advice, and the Wellcome Foundation and the Medical Research Council for financial support.

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- <sup>1</sup> Balfe, J. W., Cole, C., Smith, E. K. M., Graham, J. B., and Welt, L. G., *J. Clin. Invest.*, **47**, 4a (1968).
- <sup>2</sup> Beilin, L. J., Knight, G. J., Munro-Faure, A. D., and Anderson, J., *J. Clin. Invest.*, **45**, 1817 (1966).
- <sup>3</sup> Beilin, L. J., Knight, G. J., Munro-Faure, A. D., and Anderson, J., *J. Gen. Physiol.*, **50**, 61 (1966).
- <sup>4</sup> Siegel, S., *Nonparametric Statistics* (McGraw-Hill, Maidenhead, 1956).
- <sup>5</sup> Brewer, G. J., *Biochem. Genet.*, **1**, 25 (1967).
- <sup>6</sup> Hoffman, J. F., *J. Gen. Physiol.*, **54**, 343S (1969).

## Insect Visual Pigment sensitive to Ultraviolet Light

BEHAVIOURAL<sup>1,2</sup> and electrophysiological<sup>3</sup> experiments have shown that the insect eye responds to ultraviolet irradiation. In the eye of the honeybee there is only a small population of special ultraviolet receptors, which are involved in colour vision. In the compound eye (superposition type) of *Ascalaphus macaronius* Scop. (Neuroptera, Ascalaphidae) there are two different morphological spheres. The so called frontal eye is sensitive only to ultraviolet radiation, whereas the lateral eye also responds to green light<sup>4</sup>. For this reason, the frontal eye seemed to us a suitable source from which to try to extract the ultraviolet-sensitive photopigment of an insect.

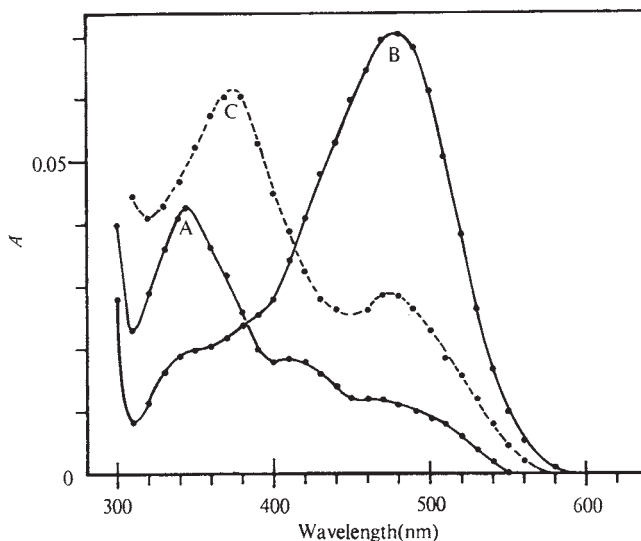


Fig. 1 The absorbance of the ultraviolet photopigment and its products. A, Original ultraviolet sensitive pigment with a peak at 345 nm; when irradiated with 354 nm (pH 5.2), A is converted to B with  $\lambda_{\text{max}}$  480 nm; a change in pH to 9.3 yields the alkaline product C with a peak at 375 nm.

The heads of dark-adapted insects were dissected and frozen. Under dim red light, the retinulae of the frontal eyes were prepared and cleaned mechanically from the screening pigments. The isolated retinulae were purified by a modified method used by us for cephalopods<sup>5</sup>, and extracted with 2% digitonin solution (pH 5.2). The most purified extract shows a small absorbance at  $345 \pm 2$  nm (Fig. 1). This pigment we shall call A. It is uncertain whether the absorbance in the range between 400 and 600 nm belongs to A or to very small impurities from the screening pigments. The ultraviolet peak corresponds to the electrophysiologically determined spectral sensitivity of the frontal eye (Fig. 3, curves 1 and 2). This is the first essential if A is to be held responsible for the

ultraviolet sensitivity of the eye. On irradiation with ultraviolet (323, 337, 354 and 370 nm) the absorbance falls in the ultraviolet region, and increases in the visible range, maximally at 480 nm (Fig. 1, curve B). If now illuminated with light of longer wavelengths (440, 483 nm), the new product B is completely reconverted (Fig. 2). This experiment can be repeated indefinitely. If the pH of an ultraviolet-irradiated solution is changed step by step from 5.2 to 9.3 in the dark, the absorbance at 480 nm decreases continuously, while the absorbance at 375 nm increases proportionately, because of the formation of a third pigment C (Fig. 1). When the pH is restored to 5, absorbance at 480 nm is regained.

In all test conditions (+20° C, pH 5–9.3), pigments A, B and C were thermostable. When an ultraviolet-irradiated solution was heated to 70° C in the presence of hydroxylamine, there was a rapid decay in absorbance at 480 nm and a rise at 360 nm. This is good evidence that the pigment has retinal as its prosthetic group ( $\lambda_{\max}$  of retinal-oxime is at 360 nm).

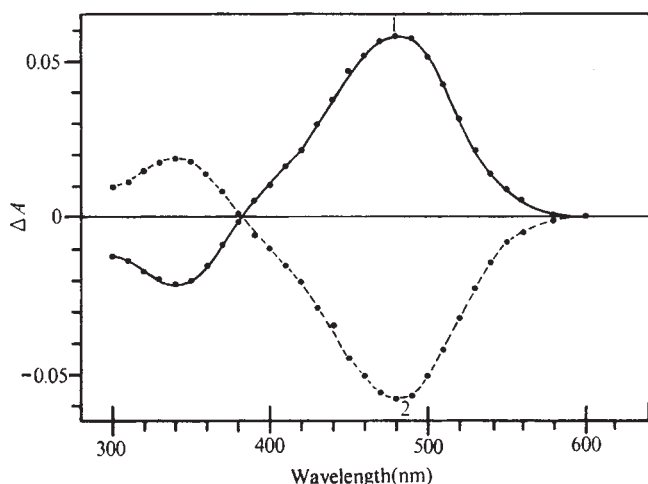


Fig. 2 Difference spectra between the photopigment A and the photoproduct B. Curve 1 is obtained by subtracting B from A; curve 2 shows the difference spectrum between B and the product after illumination with 483 nm. The identical shape of the two curves demonstrates the complete photo-inter-conversion of the two pigments.

In these characteristics, the ultraviolet-sensitive pigment resembles the visual pigments of the cephalopods, in which illumination converts rhodopsin into a pH-dependent mixture of thermostable acid and alkaline metarhodopsin<sup>5,6</sup>. In the case of the cephalopods the photoconversion and reversion from rhodopsin to acid metarhodopsin have the same relative quantum efficiencies<sup>7</sup>. With continuous monochromatic illumination, the equilibrium depends only on the specific absorption coefficients of the two pigments. Corresponding experiments on the ultraviolet-sensitive pigment show that there is also a photochemical equilibrium between A and B, but the quantum efficiencies for  $A \rightarrow B$  and  $B \rightarrow A$  must be different. Fig. 3 illustrates the change of absorbance measured at 480 nm as a function of the wavelength of irradiation compared with the absorbance of pigment A; the conformity of the two curves demonstrates that the photochemical equilibrium between A and B is determined chiefly by the absorbance of A. The curve B, produced after illumination of A with light of wavelength 354 nm, looks like an extremely purified visual pigment; the ratio of  $\epsilon_{\max}$  of A to the  $\epsilon_{\max}$  of B is 1 : 1.6 (in cephalopods the ratio rhodopsin to acid metarhodopsin is 1 : 1.43 (ref. 7)). Therefore, the content of pigment A must be very low in the illuminated solution B. This would mean that the quantum efficiency for  $A \rightarrow B$  is much higher than for  $B \rightarrow A$ . If the quantum efficiencies were equal, the absorbance of B at 480 nm should have nearly the same value as A.

Microphotometric measurements on single rhabdoms of the isolated retinula confirm these results. Irradiation with monochromatic ultraviolet light results in an increase of absorbance in the visible range; subsequent illumination with visible light reduces the absorbance to the starting point. These photochemical reversals can be observed repeatedly with only a small loss. The change of absorbance as a function of the wavelength of irradiation (curves 3 and 4, Fig. 3) is similar in shape to the absorbance of A. The time taken to reach the equilibrium value depends on the intensity of the illumination and follows a first order reaction.

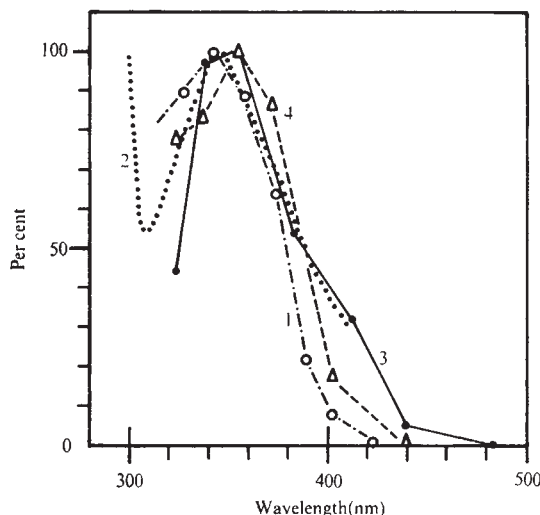


Fig. 3 The relationship between spectral sensitivity of the eye (curve 1), absorbance of the photopigment (curve 2) and the yield of photopigment B with wavelength of illumination in solution (curve 3) and in the isolated retinula (curve 4).

The conformity of all these results indicates that, because in the Sun's spectrum there is much more light in the range 400 to 600 nm than in the ultraviolet, all pigment molecules that have caught ultraviolet quanta will be very quickly reconverted by catching visible light quanta. In this way, without any chemical regeneration, the content of the ultraviolet pigment in the receptor (and thus the sensitivity) will always be nearly maximal.

This work was supported by the Deutsche Forschungsgemeinschaft and the SBK and SFNR-fonds of Yugoslavia.

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- <sup>1</sup> Frisch, K. v., *Zool. Jb. Abt. allg. Zool. Physiol.*, **35**, 1 (1914).
- <sup>2</sup> Kühn, A., *Z. Vergl. Physiol.*, **5**, 762 (1927).
- <sup>3</sup> Autrum, H., and Zwehl, V. v., *Z. Vergl. Physiol.*, **48**, 357 (1964).
- <sup>4</sup> Gogala, M., *Z. Vergl. Physiol.*, **57**, 232 (1967).
- <sup>5</sup> Hamdorf, K., Schwemer, J., and Täuber, U., *Z. Vergl. Physiol.*, **60**, 375 (1968).
- <sup>6</sup> Hubbard, R., and Kropf, A., *Proc. US Nat. Acad. Sci.*, **44**, 130 (1958).
- <sup>7</sup> Schwemer, J., *Z. Vergl. Physiol.*, **62**, 121 (1969).



## New Nitrogenase Model for Reduction of Molecular Nitrogen in Protonic Media

In enzymatic nitrogen fixation<sup>1</sup> the reducing agent, although comparatively weak, is strong enough to form hydrogen from water. Presumably metal ions (molybdenum and iron) participate in the process, the former in the activation of N<sub>2</sub> and the latter in electron transfer from the reducing agent, for example, Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub>, to the activated nitrogen molecule.

We attempted to reduce nitrogen in protonic media in the presence of molybdenum compounds by reagents with reduction potentials comparable with that of Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> and able to reduce water with the formation of H<sub>2</sub>, that is Ti<sup>3+</sup> (in alkaline solutions) Cr<sup>2+</sup> and V<sup>2+</sup> ions. The formation of hydrazine would be expected to be the first intermediate step<sup>2,3</sup>.

We have observed the reduction of molecular nitrogen in aqueous and alcohol solutions<sup>4-6</sup> which we regard as a close model of biological nitrogen fixation. The results of several experiments are presented in Table 1.

The reduction of N<sub>2</sub> in protonic solvents definitely differs from Volpin-Shur reactions<sup>9,10</sup>, in which strong reducing agents transform N<sub>2</sub> into complex nitrides in aprotic media in the presence of many transition metal compounds. We found that only vanadium compounds (for example, VOCl<sub>2</sub>) were capable of replacing molybdenum with positive results, other metal derivatives (WCl<sub>6</sub>, KReO<sub>4</sub>, FeCl<sub>3</sub> and so on) being inactive.

Moreover, V<sup>2+</sup> salts could reduce nitrogen without molybdenum compounds, and it is V<sup>2+</sup> compounds that form the most active systems for reducing molecular nitrogen. The fast reduction of N<sub>2</sub> was observed in alkaline water solutions at room temperature and at atmospheric pressure.

Specificity of Mo and V is of particular interest because, of the many metals tested, only vanadium compounds can replace molybdenum in enzymatic N<sub>2</sub> fixation<sup>11</sup>.

Table 1 shows that Mg<sup>2+</sup> ions strongly activate the reduction especially for pure Ti<sup>3+</sup> and V<sup>2+</sup> reactions. (Mg<sup>2+</sup> ions are known to take part in enzymatic N<sub>2</sub> fixation as well. But there is no evidence for a direct analogy for the role of Mg<sup>2+</sup> in enzymatic and model systems as Mg<sup>2+</sup> is required as a cofactor

**Table 1** Reduction of Molecular Nitrogen

| Red.<br>(mmol × 10 <sup>2</sup> )                                                 | Mo<br>(mmol × 10 <sup>2</sup> ) | MgCl <sub>2</sub><br>(mmol × 10 <sup>2</sup> ) | KOH<br>(mmol) | PN <sub>2</sub><br>(atm) | <i>t</i> (°C) | Time<br>(min) | N <sub>2</sub> H <sub>4</sub> *<br>(mmol × 10 <sup>5</sup> ) | NH <sub>3</sub><br>(mmol × 10 <sup>5</sup> ) |
|-----------------------------------------------------------------------------------|---------------------------------|------------------------------------------------|---------------|--------------------------|---------------|---------------|--------------------------------------------------------------|----------------------------------------------|
| Red. Ti <sup>3+</sup> ; CH <sub>3</sub> OH + H <sub>2</sub> O (5.5 : 1 mol parts) |                                 |                                                |               |                          |               |               |                                                              |                                              |
| 30                                                                                | None                            | 15                                             | 12.8          | 100                      | 85            | 10            | 2                                                            |                                              |
| 40†                                                                               | 0.0008                          | None                                           | 7.7           | 120                      | 95            | 15            | 70                                                           |                                              |
| 30†                                                                               | 0.008                           | None                                           | 9             | 20                       | 95            | 15            | 37                                                           |                                              |
|                                                                                   |                                 |                                                |               |                          |               |               | 35.2‡                                                        | 23‡                                          |
| 30                                                                                | 0.03                            | None                                           | 12.8          | 100                      | 85            | 10            | 3                                                            |                                              |
| 30                                                                                | 0.03                            | 15                                             | 12.8          | 50                       | 85            | 20            | 34                                                           |                                              |
|                                                                                   |                                 |                                                |               |                          |               |               | 33.5‡                                                        | 3.8‡                                         |
| 30                                                                                | 0.3                             | 15                                             | 12.8          | 100                      | 85            | 10            | 600                                                          |                                              |
| Red. Cr <sup>2+</sup> ; CH <sub>3</sub> OH + H <sub>2</sub> O (5.5 : 1 mol parts) |                                 |                                                |               |                          |               |               |                                                              |                                              |
| 10                                                                                | 1                               | 100                                            | 2.5           | 100                      | 85            | 15            | 150                                                          |                                              |
| 20                                                                                | 2                               | 100                                            | 2.5           | 20                       | 20            | 720           | 37                                                           |                                              |
| Red. V <sup>2+</sup> ; H <sub>2</sub> O                                           |                                 |                                                |               |                          |               |               |                                                              |                                              |
| 10                                                                                | None                            | None                                           | 42            | 1                        | 20            | 1             | Traces                                                       |                                              |
| 10                                                                                | None                            | 50                                             | 42            | 100                      | 20            | 1             | 2,200                                                        |                                              |
| 10                                                                                | None                            | 500                                            | 56            | 1                        | 20            | 1             | 320                                                          | < 20                                         |
| 10                                                                                | None                            | 500                                            | 40            | 0.9                      | 70            | 1             | Traces                                                       | 430‡                                         |

\* The analysis on N<sub>2</sub>H<sub>4</sub> was performed by means of reaction with *p*-dimethylaminobenzaldehyde<sup>8</sup>.

† Initial reagent Ti<sup>3+</sup> solution TiCl<sub>3</sub> in aqueous HCl stored under air; in other cases solution was prepared by dissolving pure Ti (met) in HCl.

‡ Mass spectroscopic analysis; <sup>15</sup>N<sub>2</sub> was used for reduction.

The principal product is hydrazine, although N<sub>2</sub> can be reduced to ammonia at higher temperatures. Thus in our experiments the first 4-electronic reduction preceded the secondary reduction of hydrazine to NH<sub>3</sub>. Although no hydrazine has been detected so far in biological fixation, there is some evidence of a transition metal-bound intermediate, which could be hydrazine<sup>7</sup>.

The reduction by Ti<sup>3+</sup> and Cr<sup>2+</sup> proceeds only in the presence of molybdenum compounds (for example, MoOCl<sub>3</sub>, MoO<sub>4</sub><sup>2-</sup>). Small amounts of hydrazine in the absence of the latter are possibly a result of the small amounts of Mo present as the impurity in the reagents.

of adenosine triphosphate (ATP) which participates in the electron activating system in N<sub>2</sub>ase<sup>1</sup>.) Other ions, such as Ca<sup>2+</sup>, Ba<sup>2+</sup>, TiO<sub>2</sub><sup>+</sup>, have similar but somewhat smaller effects. The presence of some Ti (IV) compound is probably the reason for the activity of usual Ti<sup>3+</sup> in HCl aqueous solutions which were stored in air with no Mg<sup>2+</sup> present.

Carbon monoxide strongly inhibits the reduction of N<sub>2</sub>. It is interesting that for the Ti<sup>3+</sup>-Mo system the inhibiting effect of CO was found to be quantitatively very close to that in enzymatic fixation.

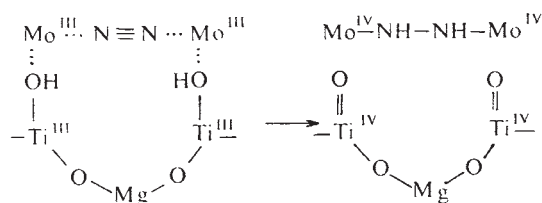
The reduction of N<sub>2</sub> proceeds only at pHs greater than 7. Alkalinity can be assumed to play a dual role. On the one

hand, the necessary structure of the active centres is obtained in hydroxides (see the diagrams), and on the other hand, the difference between the reduction potentials of reducing ion and that of hydrazine presumably increases with an increase of pH.

The molybdenum compounds are true catalysts in the reduction of nitrogen by means of  $Ti^{3+}$  at sufficiently high temperatures (Table 1), many molecules of  $N_2H_4$  being formed for each molybdenum atom. Information concerning the oxidation state of molybdenum in the active complex was obtained by investigation of the reaction, with carbon monoxide substituted for  $N_2$ . In the presence of  $CO$ , the yellow carbonyl complex of Mo (III) is formed in solution ( $\lambda_{max}=405$  nm) in the process of reduction of Mo compound by  $Ti^{3+}$  in alkaline media. Therefore, some Mo (III) compound can be assumed to be catalytically active towards  $N_2$ . This view is supported by the fact that  $V^{2+}$  activates (and reduces) nitrogen in the absence of Mo compound. Presumably, electronic state  $d_3$  corresponding to both V (II) and Mo (III) is suitable for the formation of active intermediates with molecular nitrogen.

The role of reducing agents ( $Ti^{3+}$ ,  $Cr^{2+}$ ) is probably not limited by reduction of the initial Mo (V) or Mo (VI) compound. Thus Mo (III) compounds alone were found to be unable to reduce molecular nitrogen. On the other hand, acetylene reacts with alkaline solutions containing  $Ti^{3+}$ ,  $V^{2+}$  and  $Cr^{2+}$  in the absence of a Mo compound, with the formation of ethylene. The reducing ions may therefore take part in electron transfer to the activated NN bond. Acetylene is reported<sup>12</sup> to have been reduced by certain complexes of molybdenum; the activity towards nitrogen has also been mentioned briefly. It may be seen, however, that the ability to reduce acetylene to ethylene is by itself insufficient evidence for activity towards  $N_2$ .

The participation of  $Mg^{2+}$  ions shows that the active centres must have a definite structure for activation and reduction of molecular nitrogen. The maximum activity of the titanium-molybdenum system is reached when the ratio of  $Mg^{2+}$  to  $Ti^{3+}$  is 0.5. With this in mind, the following tentative mechanism can be suggested:



The determination of the exact mechanism of the reactions requires more careful examination, but it certainly is not as complicated as the mechanism of enzymatic nitrogen fixation.

Therefore we hope that the further investigation of the model reactions will help to clarify the mechanism of enzymatic fixation of molecular nitrogen as well.

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Received November 16, 1970; revised January 18, 1971.

- <sup>1</sup> Hardy, R. W. F., and Burns, R. C., *Ann. Rev. Biochem.*, **37**, 331 (1968).
- <sup>2</sup> Lichtenshtein, G. I., and Shilov, A. E., *Zhur. Fiz. Khim.*, **44**, 849 (1970).
- <sup>3</sup> Borodko, Yu. G., and Shilov, A. E., *Uspekhi Khim.*, **38**, 761 (1969).
- <sup>4</sup> Denisov, N. T., Shuvalov, V. F., Shuvalova, N. I., Shilova, A. K., and Shilov, A. E., *Kinet. Kataliz.*, **11**, 813 (1970).
- <sup>5</sup> Denisov, N. T., Efimov, O. N., Shuvalova, N. I., Shilova, A. K., and Shilov, A. E., *Zhur. Fiz. Khim.*, **44**, 2964 (1970).

- <sup>6</sup> Denisov, N. T., Shuvalov, V. F., Shuvalova, N. I., Shilova, A. K., and Shilov, A. E., *Dokl. Akad. Nauk SSSR*, **195**, 879 (1970).
- <sup>7</sup> Jackson, E. K., Parshall, G. W., and Hardy, R. W. F., *J. Biol. Chem.*, **243**, 4952 (1968).
- <sup>8</sup> Watt, G. V., and Chrisp, J. D., *Anal. Chem.*, **24**, 2006 (1952).
- <sup>9</sup> Volpin, M. E., and Shur, B. V., *Nature*, **209**, 1236 (1966).
- <sup>10</sup> Volpin, M. E., Ilatovskaja, M. A., and Shur, B. V., *Kinet. Kataliz.*, **11**, 333 (1970).
- <sup>11</sup> Burk, D., and Horner, C. K., *Trans. Third Intern. Cong. Soil Sci.*, Oxford, **1**, 152 (1935).
- <sup>12</sup> Schrauzer, G. N., and Schlesinger, G., *J. Amer. Chem. Soc.*, **92**, 1808 (1970).

## Energetical Structure of Zoological Systems

Two problems in evolution are of continuing interest to biologists. These problems arise in connexion with the development of the special peculiarities which allow closely related species to exist side by side. If the process of evolution is regarded as a struggle for energy, a logical explanation may be found on the basis of the energetics of different species. The fact that the size of an animal is related in some way to its energetics makes it possible to test this supposition.

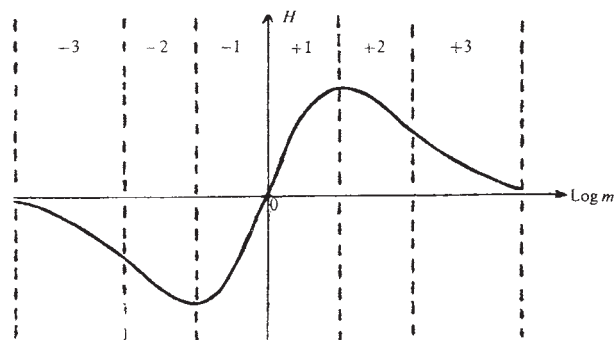


Fig. 1 The stationary conditions on the curve of the potential quasi-energy (theoretical curve).

Theoretical analysis of the dependence of the potential quasi-energy<sup>1-3</sup> on body mass reveals that the curve has five separate conditions: three turning points and two extremities (Fig. 1). If we suppose that the five separate conditions of the curve are the limits of the stationary conditions of the elements of the biosystem then the stationary conditions may be represented as six zones. It thus follows that more than six species of one genus cannot live together in one territory at the same time. Moreover, these species must differ in size.

It is well known that within a genus the curve of size distribution tends to reach a maximum close to the optimum size. This means that one genus may contain several species of similar size and quasi-energy value.

Clearly, however, these species cannot inhabit a common territory, for the principle of prohibition precludes this. We are thus led to the supposition of several "spatial orbits", each one with its own stationary conditions. The question then arises: how many stationary conditions will there be on other "spatial orbits"? To answer this question we must refer to the characteristics of the curve of size distribution, which narrows to the apex and is symmetrical in the half logarithmic scale. Clearly, the secondary orbits should arise from symmetrical narrowing of the total distribution—if there are six species on one orbit, there will be four on the next, then two and so on.

The integral function of quasi-energy is exactly equivalent but of opposite sign to the curve size distribution. Thus by simply turning everything upside down (Fig. 2), we can find three "spatial orbits": the lower orbit (2 species), the intermediate orbit (4 species) and the higher orbit (6 species). It



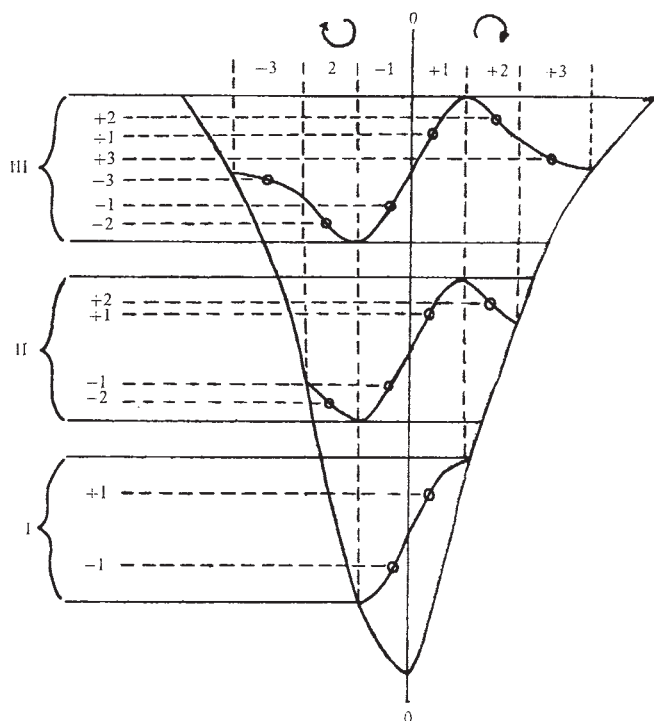


Fig. 2 The energetical structure of zoological system (diagram): 1, lower orbit; 2, intermediate orbit; 3, higher orbit.

may be supposed that the lower orbit is occupied by the most primitive species; during evolution the higher orbits were filled up.

Huxley<sup>4</sup> and Lack<sup>5</sup> were the first to analyse in detail the sizes of a genus of birds living in a common environment, and to relate the variations to their energetics (food preference). They observed that as a rule species of one genus living in the same environment contain large, medium and small sized species.

The problem of the maximum number of species able to inhabit one territory is discussed in detail by Mayr<sup>6</sup>. From his survey we see that the number of species of one genus occupying a common territory does not exceed six. Exceptions are very rare: *Parus* of Eurasia, North American *Dendroica*, *Erythro-neura* in the valley of the Mississippi, *Anopheles* in the Philippines. Sometimes five species of one genus live together, but they all differ in size.

These principles are well illustrated by Darwin's finches<sup>5</sup>. We see (Table 1) that *G. scandens* and *G. conirostris* are least

spread over the Galapagos Islands. We conclude from this that they occupy the lower orbit of the energetic level of their genus. Two predictions follow from this supposition. First, they should be phylogenetically lower than another species of this genus; and second, they must be spatially isolated from higher species phylogenetically close to them. In fact these species are the most primitive of this genus. *G. difficilis* gave rise to three species: *G. fuliginosa*, *G. fortis*, *G. magnirostris*; *G. conirostris* gave rise to *G. scandens*. *G. conirostris* and *G. scandens* are geographically isolated. *G. difficilis* is isolated from closely related species either geographically or biotopically.

Other predictions from this hypothesis are also fulfilled. For example, as I have already mentioned, the maximum number of species inhabiting one territory never exceeds six (for one genus, of course). Moreover, species occupying the lower orbit have a far more restricted size range (Fig. 3), and their sizes are accordingly approximately in the medium range for that genus. All these points are borne out by another genus of Darwin's finches—*Camarhynchus*.

Species occupying the same "spatial orbit" are characterized by relatively discrete values of quasi-energy. On the other hand species occupying different spatial orbits may be characterized by one and the same value of quasi-energy, for their orbits are discrete. Species phylogenetically earlier occupy the lower "spatial orbit", species phylogenetically later—intermediate and higher orbits. On the lower orbit more than two species cannot exist simultaneously; on the intermediate orbit, there cannot be more than four; and on the main orbit, there cannot be more than six (in cases of cohabitation on one territory). This does not, of course, eliminate the possibility of one, three or five species in an ecosystem; but in this case we can say that the "spatial orbits" are not filled up yet.

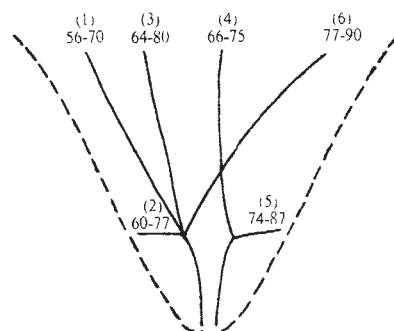


Fig. 3 The energetical structure of genus *Geospiza* (see Table 1).

This theory entails no restrictions on the number of species of a genus. It is perfectly possible that energetical levels are duplicated in other territories and time; and this may be the case for insects.

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Received April 24, 1970.

<sup>1</sup> Djulidin, A. A., and Mezherin, V. A., in *Bion. Mat. Mod.*, 1, 109 (1969).

<sup>2</sup> Mezherin, V. A., and Djulidin, A. A., *Nature* (in the press).

<sup>3</sup> Mezherin, V. A., in *Proc. IPB Meeting* (edit. by Petruszewicz, K., and Ryszkowski, L.) (in the press).

<sup>4</sup> Huxley, J. S., *Evolution, the Modern Synthesis* (Allen and Unwin, London, 1942).

<sup>5</sup> Lack, D., *Darwin's Finches* (Cambridge University Press, Cambridge, 1947).

<sup>6</sup> Mayr, E., *Animal Species and Evolution* (Harvard University Press, 1963).

Table 1 Wing Length (in mm) of Six Species of Darwin's Finches

| 1     | 2     | 3        | 4        | 5        | 6        |
|-------|-------|----------|----------|----------|----------|
| 57-61 | 61-64 | 64-72    | 72-74    |          | 79-87    |
| 60-66 | 65-76 | 69-77    | 66-72    | -        | 81-88    |
| 61-66 | 67-71 | 69-79    | 70-75    | -        | 83-86    |
| 56-61 | -     | 65-70    | 71-75    | -        | 77-85    |
| 63-67 | -     | 71-72    | 69-73    | -        | 78-90    |
| 61-70 | -     | 67-80    | 68-75    | -        | 80-83    |
| 62-68 | -     | 72-80    | is found | -        | is found |
| 61-66 | -     | is found | 68-75    | -        | is found |
| -     | 60-66 | -        | -        | 74-81    | 84-89    |
| 60-67 | -     | 65-73    | -        | -        | is found |
| 60-66 | -     | 66-75    | -        | -        | 81       |
| -     | 71-77 | -        | -        | 77-87    | -        |
| 61-67 | -     | -        | -        | 74-84    | -        |
| 60-67 | -     | 69-78    | -        | -        | -        |
| -     | 68-75 | -        | -        | -        | 84       |
| -     | -     | -        | -        | is found | -        |

These species (genus *Geospiza*) occupy a common territory: 1. *G. fuliginosa*; 2. *G. difficilis*; 3. *G. fortis*; 4. *G. scandens*; 5. *G. conirostris*; 6. *G. magnirostris*.

## Cycles in Social Behaviour

Young and Ziman, writing about *Cycles in Social Behaviour*<sup>1</sup>, suggest that "cycles of personal behaviour . . . are partly governed by endogenous biological mechanisms which need to be sustained by food and sleep at more or less regular intervals".

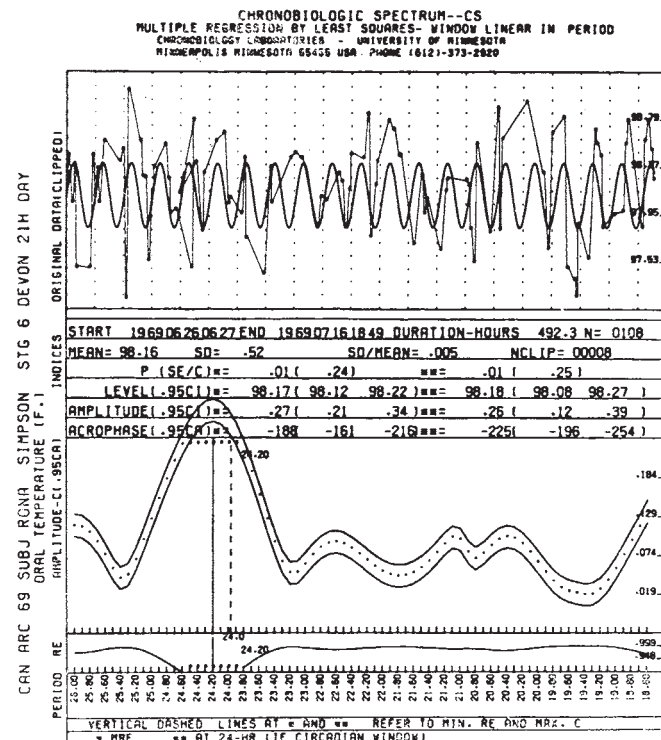


Fig. 1 1969 Canadian Arctic 21 h day survey in Devon Island. Oral temperature of one subject (Rona Simpson) aged 7. At top, 3 weeks raw data in °F with overprint of best fit cosine wave in spectrum 26.0 h to 18.6 h with 0.2 h interval. At bottom, serial amplitudes with the 0.95 confidence limits. Also residual error (r.e.) the minimum of which indicates best fit.

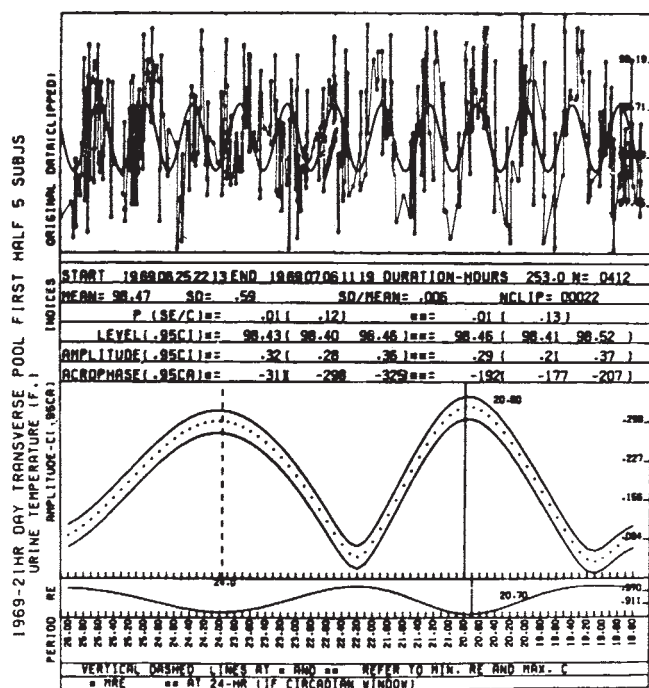


Fig. 2 Same study as Fig. 1. Urine temperature data of remaining subjects (3 adults, 2♂ + 1♀, and 2 boys aged 8 and 9) for first 1½ weeks of 3 week 21 h "day" study. There are two best fit frequencies in the circadian spectrum—one of the presumed endogenous component (about 24 h) and the other at the environmental frequency.

With others, I have made extensive studies of the effect of a 21 h "day" (8 "days" per calendar week) on human circadian rhythms. One object of such studies is to separate circadian rhythms into environment and/or endogenous components. In these circumstances human body temperature rhythm may show only an about 24 h component in a computer analysis in which cosine waves at different circadian frequencies are fitted by least squares (Fig. 1). Other subjects for this variable show a mixture of endogenous (about 24 h) and environmental components (Fig. 2) (first 1.5 weeks of 3 week study); moreover, this amplitude ratio (about 24.0 h/21.0 h) did not change appreciably in the second 1.5 weeks of the study (Fig. 3).

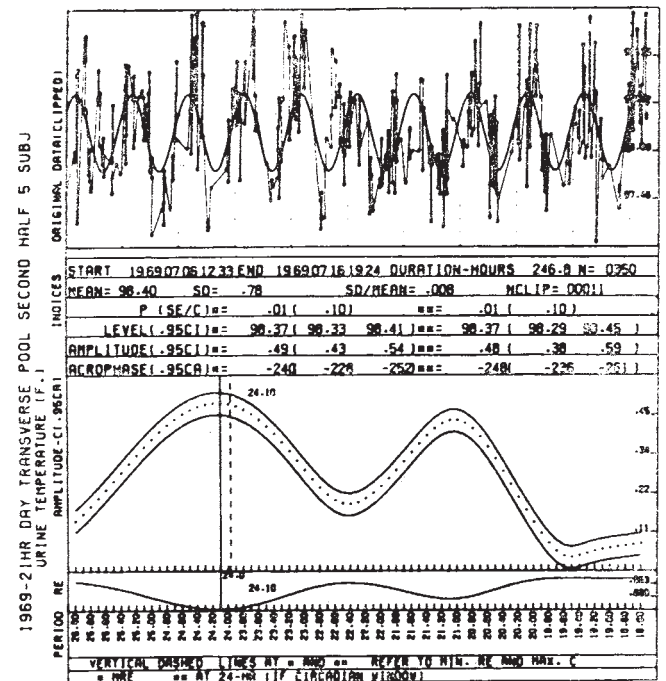


Fig. 3 Same study and subjects as Fig. 2. Second 1½ weeks of 3 week 21 h study. Two frequencies emerge as in Fig. 2 and the greater amplitude is the endogenous component. This is the opposite of what one would expect if it required an input from the routine to sustain it.

In other words, the endogenous biological mechanism for this rhythm (and for review of others see ref. 2) does not necessarily need to be sustained by food and sleep.

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Received January 18, 1971.

<sup>1</sup> Young, M., and Ziman, J., *Nature*, 229, 91 (1971).

<sup>2</sup> Simpson, H. W., Halberg, F., and Lobban, Mary, *Arctic Anthropology*, 7, 144 (1970).

## Is the Haptic Müller-Lyer a Visual Phenomenon?

GEOMETRIC illusions of active touch, or haptic illusions, resemble their visual counterparts<sup>1-3</sup>, which suggests that a single process underlies both phenomena. Over<sup>4</sup> has argued from this that a purely visual theory such as Gregory's<sup>5</sup> is untenable because the interpretation of visual illusions in terms of depth cues is clearly inapplicable for haptic/tactile space. Gregory (*vide* Horrell<sup>6</sup>) has replied by suggesting that in a haptic illusion there is some form of cross-modal transfer (possibly involving visual imagery) such that the haptic information is dealt with centrally just as if it were visual in



origin. This can explain the similarities between visual and haptic illusions but it cannot account for the failure of both Horrell<sup>6</sup> and Fisher<sup>7</sup> to find individual difference correlations between visual and haptic forms of the same illusion. Horrell has, however, found a small though not significant correlation for subjects reporting substantial visual imagery while setting a haptic Müller-Lyer ( $r=0.39$ ,  $N=10$ ). Thus perhaps the reason for the absence of overall correlations in the Horrell and Fisher studies was that, although cross-modal transfer led to similar mean errors for each kind of illusion, most subjects were so inefficient at visualizing on the basis of feel and touch that the predicted across subject correlations were obscured. And, of course, cross-modal processes might in addition be subject to other sources of inefficiency. This "inefficiency hypothesis" predicts that subjects who are good at haptic to visual transfer (measured independently of the illusions) should provide a high between modalities illusion correlation and less able subjects a low or zero one. This experiment tests this prediction and it also investigates the possible role of visual imagery in the suggested cross-modal processes.

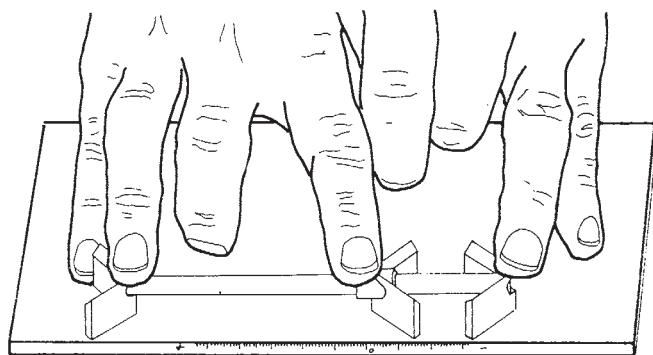


Fig. 1 An outline sketch of the haptic Müller-Lyer device showing the position of the subject's fingers. The angle between the fins was 90°, the length of each fin was 1.9 cm and the distance between the tips of the outer arrowheads was 12.0 cm.

Forty-nine subjects, whose MacKinnon<sup>8</sup> general visual imagery scores were known, first had to set a haptic Müller-Lyer (hidden by a screen) using three fingers (Fig. 1) in such a way that the point of the movable arrowhead appeared to be midway between the points of the outer fixed ones. Each subject made six such settings, three with each index finger in a counterbalanced order.

The device was then removed and replaced by another similar one except that in place of the arrowheads were three straight knife-edges arranged at right angles to the slider bar. Six "control" readings were taken with this new device and the mean of these was used in the analysis to correct the mean of the previous six for any enduring biases due to handedness, and so on. This resulted in a set of H1 scores.

The second task was a haptic to visual shape recognition test consisting of ten items. For each, the subject was required to feel freely with both hands a flat metal cut-out shape for 10 s, after which he had to drop it and select from a visually presented ensemble of six similar shapes the one which he thought he had been feeling. All the shapes were selected from the random shapes described by Vanderplas and Garvin<sup>9</sup>. Each subject was given a recognition score which was the ratio of the number of correct identifications to the average recognition time (errors excluded).

The third task required the subject to set visually (with only the index finger and thumb of his preferred hand in contact with only the movable part of the apparatus) the Müller-Lyer and straight-edge devices which up to this point he had

only felt. A corrected V1 score was thus obtained for each subject in much the same way as for the H1 measures.

The fourth task was a replication of the first. It provided a second, post-visual H2 score for each subject.

The fifth task produced a V2 score for each subject by requiring him to set visually six times an adjustable, hand held, ink on cardboard Müller-Lyer. This Müller-Lyer was similar to the haptic one both geometrically and in not having its arrowheads joined. (The subjects were not allowed to move their fingers off the haptic arrowheads and so they did not feel a line joining them. This constraint on active touch was incorporated to make any cross-modal transfer more difficult than is usual in a haptic illusion, and so more likely to reveal individual differences.)

Finally, each subject was asked to complete Horrell's<sup>6</sup> questionnaire which asked him to rate on a four point scale the visual imagery he experienced while setting the haptic figures.

Correlations between the various illusion measures were computed both for the group of subjects considered as a whole and for three pairs of "high" and "low" subgroups considered separately, each pair being selected on the basis of a different criterion measure using certain arbitrary cut-off points. The whole group data provided none of the significant positive haptic-visual correlations expected on the simple cross-modal transfer hypothesis (so replicating the findings of Horrell and Fisher) and neither did the data of the three low subgroups. But all three high subgroups supplied evidence in favour of the "inefficiency" version of the cross-modal view. (1) The most able subjects in the recognition test showed a significant correlation between their H2 and V2 settings ( $r=0.52$ ,  $N=15$ ,  $P<0.025$ ). (2) Those subjects who reported considerable visual imagery while setting the haptic figures provided a significant H2/V1 correlation ( $r=0.34$ ,  $N=28$ ,  $P<0.05$ ). (3) Those subjects high on general visual imagery also provided a significant H2/V1 correlation ( $r=0.61$ ,  $N=15$ ,  $P<0.01$ ).

Although the various subgroups overlapped in subject composition, the different criteria did not pick out a single uniform "hard-core" of good transfer subjects who were the only ones to provide the predicted haptic/visual correlations. Thus, for example, subjects with good general visual imagery who were poor on the recognition task mirrored their parent high subgroup by only showing a significant H2/V1 correlation ( $r=0.68$ ,  $N=8$ ,  $P<0.05$ ). Similarly, good recognizers with poor imagery gave the same pattern of results as the high recognition subgroup from whence they were drawn, albeit not significantly ( $r$  for H2/V2=0.50,  $N=8$ ). This suggests that of those subjects who achieved accurate cross-modal transfer, some used visual imagery and some did not.

It is also interesting that there were significant correlations only with the H2 measures, in spite of the absence of significant mean differences between the H1 and H2 settings, and the fact that all but three of the subjects realized from the outset that they were feeling a Müller-Lyer. (No references were made in the instructions to illusions—or indeed to imagery—but the subjects were familiar with the Müller-Lyer from a laboratory class experiment.) This suggests that practice or visual experience (or both) of the haptic device is necessary for the predicted relationships to emerge. This possibility fits in well with the "inefficiency hypothesis" although a proviso needs to be added: the H2 settings were made directly in between the V1 and V2 ones, whereas the H1 readings were separated from all the others by the recognition test. A future experiment will explore this question in more detail and also examine the reliability of the observation that the high imagery subgroups give correlations only with the V1 scores whereas subjects who are good at recognizing shapes do so only with the V2 readings.

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Received August 26, 1970; revised January 8, 1971.

- <sup>1</sup> Revesz, G., *J. Psychol. Psychotherapie*, **1**, 464 (1953).
- <sup>2</sup> Over, R., *Amer. J. Psychol.*, **79**, 590 (1966).
- <sup>3</sup> Rudel, R. G., and Teuber, H. L., *Quart. J. Exp. Psychol.*, **15**, 125 (1963).
- <sup>4</sup> Over, R., *Nature*, **214**, 629 (1967).
- <sup>5</sup> Gregory, R. L., *Nature*, **199**, 678 (1963).
- <sup>6</sup> Horrell, R. I., thesis, Univ. Sheffield (1968).
- <sup>7</sup> Fisher, G. H., *Nature*, **212**, 105 (1966).
- <sup>8</sup> MacKinnon, A. A., *Bull. Brit. Psychol. Soc.*, **21**, 115 (1968).
- <sup>9</sup> Vanderplas, J. M., and Garvin, E. A., *J. Exp. Psychol.*, **57**, 147 (1959).

## Visual System Anomaly associated with Albinism in the Cat

ALBINISM is associated with functional incompetence of the non-decussating optic fibres. Discovered in the Norwegian rat<sup>1</sup>, the incompetence has been confirmed and extended in behavioural, anatomical and electrophysiological studies of rats and rabbits<sup>2-5</sup>. Because sensory-neural deficiencies have also been observed in human albinos<sup>6</sup>, it is possible that this anomaly of the visual pathway is a highly general, trans-species phenomenon. To obtain further evidence, I performed electrophysiological studies on both the natural-population feline and its Siamese (that is, albinic) counterpart<sup>7</sup>.

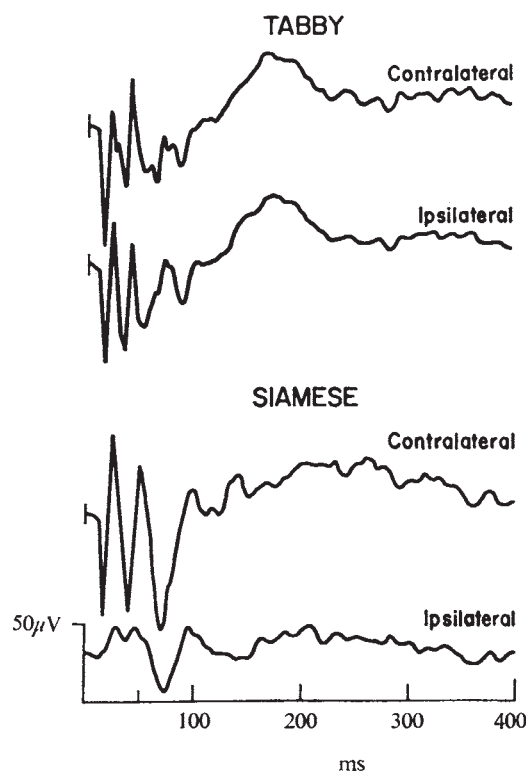
Five Siamese cats and six "tabbies" were anaesthetized with 'Nembutal' and then individually placed in a stereotaxic instrument equipped with an analogue mapping system<sup>8</sup>. Electrical activity evoked by a Grass PS2C photic stimulator was recorded from primary and secondary areas of exposed visual cortex through the electrode and an indifferent lead on the midline. These electrodes were connected to an amplifier of a Grass 6 polygraph that was coupled to a Fabri-Tek 1052-LSH signal averager, which was set to sum time-locked cortical potentials over 500 ms at the presentation of each photic stimulus. Single responses, or a series of summed evoked responses, were recorded on a Mosely X-Y plotter. At the locus where the strongest primary response was observed in the right hemisphere of each cat, a chronic electrode was placed; so, too, for the homologous locus over the left hemisphere. Each of the bilateral electrodes as well as the indifferent lead consisted of a 5 mm stainless steel screw threaded through the calvarium to touch the dura with a contact surface of approximately 2 mm<sup>2</sup>. The indifferent lead was at stereotaxic atlas coordinates A-25, L-O<sup>9</sup> in all animals; primary recording electrodes ranged anteriorly across the animals from +3 to -2 mm, with respect to the interaural line and were lateral to the midline at (left to right) 3 mm. The electrode leads, formed from a length of enamelled nichrome wire, were pre-soldered at one end to an electrode screw, and at the other to the pins of a miniature Cannon plug. The plug served as a connecting pedestal and was secured to the calvarium with dental acrylic.

After a 2 week interval for recovery from surgery, each animal was habituated daily to restraint in a hammock. During habituation and the electrophysiological measures that followed, a reflective, white plastic hemisphere 70 cm in diameter was placed with its centre in front of and 30 cm distal to the animal's eyes. The lamp of the photo-stimulator was above and behind an animal's head at 110 cm from the centre of the hemisphere. The laboratory was dark during a recording session. Pupillary motility was controlled by topical application of a 2% solution of 'Isopto Homatropine' to the cornea.

After three recording sessions per animal had been conducted over 2 weeks, the animals again underwent surgery, monocular enucleation being accomplished in each while under 'Nembutal' anaesthesia and in sterile operating conditions. After 2 more

weeks averages of evoked responses were observed over a 2 week span to blocks of 50 photic stimuli.

Finally, all five Siamese cats and two tabbies representative of the original six underwent comprehensive cortical mapping experiments by surgery. The following results were obtained: before enucleation (that is, with binocular photic stimulation) strong responses were evoked from each hemisphere but did not differ in any animal with respect to laterality or strain; following enucleation, monocularly evoked responses were observed in strength on the contralateral cortex but were unequivocally diminished on the ipsilateral cortex of all five Siamese cats. All six tabbies, in contrast, continued to have strong primary responses on both hemispheres. The evoked responses recorded from the ipsilateral hemisphere of the Siamese cats were completely lacking in the primary response, the discrepancy between the hemispheres being comparable with that observed in the rat and guinea-pig<sup>5</sup> (Fig. 1).



**Fig. 1** These are evoked responses from a normally pigmented cat and from a Siamese cat following monocular enucleation. Chronic dural electrodes had previously been fitted through the calvarium, one at a locus of the visual cortex yielding the largest photic evoked response; the other at the homologous locus over the other hemisphere. Upward deflexions are electrically negative.

These findings are highly consonant with anatomical data from cats of the natural population<sup>10</sup> and with Guillery's study of Siamese cats<sup>11</sup>; although estimates of the proportion of non-crossing optic fibres in the normal cat range from 30 to 40% of the total primary optic process, the relative number was found by Guillery to be much reduced in the Siamese cat.

In cats and man, abnormalities of ocular pigmentation have been associated with the absence of the organ of Corti<sup>12</sup>. One of the many links between pigmentation defects and neurological disorders in man, the Waardenburg syndrome, includes a white forelock, differing coloration of the irises, partial albinism of skin and deaf-mutism<sup>13</sup>. Fisch reported<sup>12</sup> that the spiral ganglion of a deaf, albino child contained only a few ganglion cells, and that the eighth nerve was thin, poorly



myelinated and sparsely populated with nerve fibres. He hypothesized that the child's deafness could have resulted from the failure of nerve cells to migrate from the neural crest to the cochlea, and a number of studies have substantiated this hypothesis<sup>12</sup>. Phenotypically albinic rats and rabbits, as well as Siamese cats, possess a genetically determined reduction of non-crossing optic fibres<sup>2,4,11</sup>. The appearance of a reduced ipsilateral component together with pigmentation abnormalities suggests the neural crest as a common site of genetic action in producing the sensory-neural defects<sup>12</sup>. Genotypical albinism may be marked by ostensible presentments of pigmentation (as for the Siamese cat) giving rise to the possibility that significant numbers of experimental animals are neurologically defective or deviant. Also, the widespread investigative use of albino rats, rabbits and guinea-pigs, particularly in the neurophysiological laboratory, augurs the need for caution in generalizing data to normal strains, whose neurological make-up may differ considerably.

I thank Drs Harry Knauff and Richard L. Sutton, jun., for advice. This work was supported by the US Veterans Administration.

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Received October 13, 1970; revised January 20, 1971.

- <sup>1</sup> Sheridan, C. L., *J. Comp. Physiol. Psychol.*, **59**, 292 (1965).
- <sup>2</sup> Lund, R. D., *Science*, **149**, 1506 (1965).
- <sup>3</sup> Creel, D. J., Dustman, R. E., and Beck, E. C., *Proc. Amer. Psych. Assoc.*, **77**, 245 (1969); Creel, D. J., and Sheridan, C. L., *Psychon. Sci.*, **6**, 89 (1966); Montero, V. M., Brugge, J. F., and Beitel, R. E., *J. Neurophysiol.*, **31**, 221 (1968).
- <sup>4</sup> Giolli, R. A., and Guthrie, M. D., *J. Comp. Neurol.*, **136**, 99 (1969).
- <sup>5</sup> Creel, D. J., Dustman, R. E., and Beck, E. C., *Exp. Neurol.*, **29**, 298 (1970); Creel, D. J., Dustman, R. E., and Beck, E. C., *J. Comp. Physiol. Psychol.*, **73**, 490 (1970).
- <sup>6</sup> Brown, R. V., *J. Hered.*, **59**, 218 (1968); Reed, W. B., Stone, V. M., Boder, E., and Ziprkowski, L., *Arch. Derm.*, **95**, 176 (1967); Tietz, W., *Amer. J. Human Genet.*, **15**, 259 (1963); Woolf, C. M., Dolowitz, D. A., and Aldous, H. E., *Arch. Otolaryngol.*, **82**, 244 (1965).
- <sup>7</sup> Peltz, R. S., *Cat Fancy*, **5**, 50 (1967); Robinson, R., *Bibl. Genetica*, **18**, 273 (1959); Shaw, D. H., *J. Cat Genet.*, **1**, 16 (1961); Sinnott, E. W., Dunn, L. C., and Dobzhansky, T., *Principles of Genetics* (McGraw-Hill, New York, 1958).
- <sup>8</sup> Justesen, D. R., Pendleton, R. B., Porter, P. B., and Romney, R., *Psychon. Monog. Suppl.*, **1**, 207 (1966).
- <sup>9</sup> Jasper, H. H., and Ajmone-Marsan, C., *A Stereotaxic Atlas of the Diencephalon of the Cat* (National Research Council of Canada, Ottawa, 1954).
- <sup>10</sup> Guillery, R. W., *J. Comp. Neurol.*, **138**, 339 (1970); Polyak, S., *The Vertebrate Visual System* (University of Chicago Press, 1957); Stone, J., *J. Comp. Neurol.*, **126**, 535 (1966); Walls, G. L., *The Vertebrate Eye and Its Adaptive Radiation* (Cranbrook Press, Bloomfield Hills, 1942).
- <sup>11</sup> Guillery, R. W., *Brain Res.*, **14**, 739 (1969).
- <sup>12</sup> Deol, M. S., *Proc. Roy. Soc.*, **175**, 201 (1970).

## Transduction and Skeletal Evolution

It has been suggested<sup>1,2</sup> that transduction of genes by viruses was an important mechanism in evolution for spreading useful mutations between organisms not formally related. I suggest that this may be an essential part of the explanation of one of the most remarkable features of the palaeontological record, the relatively sudden and almost simultaneous appearance in the Cambrian sedimentary deposits of fossils, consisting of the mineral skeletons of animals belonging to many different phyla of the animal kingdom. If, as we must assume, these animals

are the products of divergent evolution from a common set of ancestors, the time needed for such divergence is probably to be reckoned in hundreds of millions of years. The scanty but growing record of Pre-Cambrian fossils seems to show, however, that all these animals with skeletons evolved from soft-bodied ancestors during 100 m.y. at most. This parallel and rapid evolution seems to demand a mechanism beyond the accepted processes of spontaneous mutation and natural selection.

At Ediacara, South Australia, a metazoan fauna was discovered<sup>3</sup> in the Pound Sandstone<sup>4</sup>, and Glaessner<sup>5</sup> has reviewed it and related faunas in other localities, of which ten are now known. They are as far apart as South-West Africa, Newfoundland, England and Siberia, the known ages of the strata all being between 600 and 700 m.y., and thus not more than 100 m.y. before the beginning of the fossiliferous Cambrian period. The Ediacara fauna remains by far the richest of all, however, with about thirty distinct species, almost all very different from any known in the Cambrian. There are no known beds with fossils of the kinds occurring at Ediacara inter-stratified with beds containing Cambrian faunas. It seems, therefore, that soft bodied animals evolved in 100 m.y. or less into animals with mineral skeletons, belonging to numerous phyla most of which still exist. Calcified skeletons must have evolved within the same relatively short time in a wide range of phyla which had already evolved separately for a very much longer time.

It is known that early skeletons in most phyla consist of phosphate rather than carbonate<sup>6</sup>, and that the site of deposition of skeletal phosphate is characterized by the presence of large amounts of alkaline phosphatase. Thus we can assume that the evolution of a protein with phosphatase activity was an important part of the initiation of skeletal development.

The way in which phosphatase acts in the deposition of skeletal phosphate is more complex than had been supposed<sup>7</sup>; the enzyme also seems to be necessary for the deposition of the carbonate type of skeleton which evolved later. If the acquisition of phosphatase was the principal determining factor in the ability to build a calcium salt skeleton, then within a geologically short space of time, about  $6 \times 10^8$  yr ago, numerous phyla evolved such an enzyme. If the formation of the gene for such an enzyme had been the result of a fairly probable chance mutation from a previously existing common gene, we might have expected it to occur and become functional at a much earlier stage in the evolution of the metazoa, so that all phyla able to use skeletons would have developed them at an early stage in their evolution. On the other hand, if the occurrence was highly improbable, depending, for example, on simultaneous mutations of numerous DNA units, then we would expect it to have occurred at widely different times in different phyla. Its probable almost simultaneous appearance in numerous phyla  $2 \times 10^9$  yr after the beginning of organic evolution suggests that the gene responsible, whether it gave rise to phosphatase or some other enzyme or protein, was the result of a highly improbable mutation, but that, having occurred, it was transmitted to all or most metazoan phyla in the course of a relatively few million years. This cannot, of course, have taken place by ordinary sexual reproduction, but I suggest that, having once proved successful, and presumably spread to the whole of the species in which it first occurred, the mutation continued to spread to virtually the whole of the metazoa and parazoa by means of transduction. If so, viruses must have existed, and played an important part in organic evolution, at least since the beginning of Phanerozoic time.

I thank Dr N. G. Anderson, Professors M. F. Glaessner and K. Simkiss, and Dr P. H. A. Sneath for discussions.

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Received January 19; revised March 8, 1971.

- <sup>1</sup> Sokal, R., and Sneath, P. H. A., *Principles of Numerical Taxonomy*, 72 and 226 (Freeman, San Francisco and London, 1963).  
<sup>2</sup> Anderson, N. G., *Nature*, **227**, 1346 (1970).  
<sup>3</sup> Sprigg, R. C., *Trans. Roy. Soc. South Austral.*, **71**, 212 (1947).  
<sup>4</sup> Glaessner, M. F., and Wade, M., *Palaeontology*, **9**, 599 (1966).  
<sup>5</sup> Glaessner, M. F., *Bull. Geol. Soc. Amer., Notes and Discussions* (in the press, 1971).  
<sup>6</sup> Glaessner, M. F., *Biol. Rev.*, **37**, 467 (1962).  
<sup>7</sup> Simkiss, K., *Biol. Rev.*, **39**, 487 (1964).

## Effect of PCB on Nocturnal Activity in Caged Robins, *Erithacus rubecula* L.

CHLORINATED hydrocarbons are a recognized threat to populations of wild birds, but their precise mode of ecological action is largely unknown. They are, however, known to have a thinning effect on the egg shell<sup>1,2</sup>, and they react with some hormones<sup>3,4</sup>, thus affecting the endocrine balance of the body. Such findings suggest that these substances may exert a profound influence on the activity and behaviour of contaminated animals, but little attention has been devoted to this aspect.

The migratory activity of birds is governed chiefly by the interplay of hormonal systems<sup>5,6</sup>, and the orientation of the migrants is a highly refined instinct pattern. This suggests that the nocturnal activity of affected migratory birds might be a suitable indicator of the possible ecological effects of organochlorines.

The robin, *Erithacus rubecula* L., in Sweden is almost completely migratory, moving exclusively by night. Its main flight direction during the autumn migration is SW-SSW. Robins were trapped at Falsterbo Bird Station (55° 23' N, 12° 50' E) in the last week of September 1970. They were kept singly in opaque plastic containers under a natural light-dark rhythm and were fed mealworms and berries *ad lib*. Beginning on October 2, twenty-eight robins were given one extra mealworm each day, injected with 5 µg of 'Clophen A50', a polychlorinated biphenyl (PCB). These worms were marked with a small dot of red dye to enable us to determine whether the worm had been eaten; in a few cases it was not taken. Eighteen robins were kept in identical conditions but were not given worms containing PCB.

The experiments were performed between 1900 and 2100 on October 21 and 22 (within the normal migratory period of Swedish robins) on birds which had eaten eleven to thirteen PCB-loaded worms. The experimentally contaminated and control birds were placed singly in Emlen funnels under the open sky at a site 20 km east of Lund, where no artificial light sources interfered. During the first night the sky was overcast, and the experiment was discontinued after 35 min because of rain. During the second night, cloud-cover was approximately 1/8, and the experiment was continued for 75 min as planned. The evaluation of the activity sums and of the mean vectors of the birds followed the procedures described by Raböl<sup>7,8</sup>. On the first occasion, twenty PCB-loaded and twelve control birds were tested, and on the second, nineteen and eleven birds, respectively. With a few exceptions, the same individuals were used in both experiments.

The average activity sums were compared separately for each night using a Mann-Whitney U test (two-tailed). The average activity on the first night was much higher in the PCB-loaded birds than in the controls, but the difference was not quite significant. On the second night, when the experiment ran for a longer period, the average activity of the PCB-loaded birds was significantly higher than that of the controls ( $P < 0.05$ ). The dispersion of the mean vectors was greater on the overcast night of October 21 than on the following night which was cloudless. No significant differences between PCB-loaded and control birds with respect to direction or dispersion were detected on either night. The direction was the same as the supposed standard migratory direction of Swedish robins.

The age<sup>9</sup> and body weight of control and PCB-loaded birds were compared, and no significant differences were found. Both groups had gained weight equally by comparison with birds weighed immediately after trapping at Falsterbo<sup>10</sup>.

**Table 1** Organochlorine Residues (ng/g Fresh Weight) in Breast Muscles of Robins

|                    | µg of PCB ingested | <i>p,p'</i> -DDE | <i>p,p'</i> -DDT | PCB |
|--------------------|--------------------|------------------|------------------|-----|
| Birds fed with PCB | 60                 | 95               | 7                | 375 |
|                    | 55                 | 96               | 25               | 467 |
|                    | 65                 | 75               | 25               | 341 |
|                    | 55                 | 64               | 24               | 164 |
|                    | 60                 | 91               | 22               | 365 |
|                    | 55                 | 56               | 2                | 287 |
| Control birds      | —                  | 72               | 23               | 120 |
|                    | —                  | 69               | 27               | 70  |
|                    | —                  | 70               | 30               | 90  |
|                    | —                  | 66               | 25               | 51  |

The breast muscles of six PCB-loaded birds and four control birds were analysed by gas chromatography for organochlorine content (Table 1). The apparatus consisted of a Varian Aerograph 204 gas chromatograph equipped with electron capture detectors, and three different columns using SF 96 (4%), QF I (8%) and SF 96/QF I (3:1) as the stationary phases on GasChrom P (100/120 mesh) were utilized. The identity of the more important compounds detected was also confirmed by chemical techniques. The PCB level in the experimentally contaminated birds was four times that found in the controls, the difference being statistically highly significant, but it was in unexpectedly low concentration, indicating that much of it had been excreted or stored elsewhere than in the breast muscles. Both groups of birds were also analysed for *p,p'*-DDE and *p,p'*-DDT, but no significant differences were detected.

These results demonstrate an effect of organochlorine residues on the activity patterns of the bird. Gwinner<sup>11</sup> demonstrated a correlation between the degree of migratory activity (restlessness) and the distance between the breeding and wintering quarters in different warbler species of the genus *Phylloscopus*. A quantitative change in such activity therefore assumes great ecological significance. The rapid mobilization of fat during migration is also an important aspect of this problem<sup>12,13</sup>.

PCB compounds occur widely in the global ecosystem and, like other chlorinated hydrocarbons, they accumulate in food chains<sup>14,15</sup>. Their effects, even at the relatively low levels used in these experiments, indicate that they are important environmental contaminants.

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- <sup>1</sup> Ratcliffe, D. A., *J. Appl. Ecol.*, **7**, 67 (1970).
- <sup>2</sup> Peakall, D. B., *Science*, **168**, 592 (1970).
- <sup>3</sup> Peakall, D. B., *Nature*, **216**, 505 (1967).
- <sup>4</sup> Lincer, J. L., and Peakall, D. B., *Nature*, **228**, 783 (1970).
- <sup>5</sup> Farner, D. S., *Proc. XIV Intern. Orn. Cong. Oxford, 1966*, 107 (Blackwell, Oxford and Edinburgh, 1967).
- <sup>6</sup> Berthold, P., *Zool. Jb. Syst.*, **96**, 491 (1969).
- <sup>7</sup> Rabøl, J., *Orn. Scand.*, **1**, 27 (1970).
- <sup>8</sup> Rabøl, J., *Dansk Orn. For. Tidsskr.*, **64**, 118 (1970).
- <sup>9</sup> Svensson, L., *Identification Guide to European Passerines* (Naturhist. Riksmus., Stockholm, 1970).
- <sup>10</sup> Scott, R. E., *Vår Fågelv.*, **24**, 156 (1965).
- <sup>11</sup> Gwinner, E., *J. f. Orn.*, **109**, 70 (1968).
- <sup>12</sup> Helms, C. W., *Amer. Zool.*, **8**, 151 (1968).
- <sup>13</sup> Hussell, D. J. T., *Auk*, **86**, 75 (1969).
- <sup>14</sup> Risebrough, R. W., Rieche, P., Peakall, D. B., Herman, S. G., and Kirven, M. N., *Nature*, **220**, 1098 (1968).
- <sup>15</sup> Jensen, S., Johnels, A. G., Olsson, M., and Otterlind, G., *Nature*, **224**, 247 (1969).

## Skua Numbers and Conservation Problems at Cape Hallett, Antarctica

THE flora and fauna of Antarctica are often considered to be secure, principally because of international treaty obligations. Nevertheless, several people have already drawn attention to conservation problems<sup>1-3</sup>, which are underlined by my own work on the decline of the South Polar skua (*Catharacta maccormicki*) at Cape Hallett (lat. 72° 18' S, long. 170° 19' E).

During the two austral summers of 1967-68 and 1968-69, I made an intensive study of the decline of the skua and of skua-penguin feeding relationships, which will be published in full later. Data gathered by Dr T. S. Choate in the 1966-67 season are also incorporated in this report.

Because of the scarcity of suitable coastal building sites, man sometimes competes directly with nesting birds for space. In December 1956, for example, when the joint United States-New Zealand station was established, 3,318 juvenile and at least 4,900 adult Adelie penguins (*Pygoscelis adeliae*) were removed from the Hallett rookery<sup>4</sup>, and at that time the breeding population was probably between 56,000 and 62,000 pairs<sup>5</sup>.

Although indications of the size of the resident skua breeding population are available<sup>4,6</sup>, the first census was of 181 pairs in the 1960-61 season<sup>7</sup>. Census records in subsequent seasons reveal a drastic decline in the numbers of skua pairs breeding; these are 162 pairs in 1963-64 and 147 pairs in 1965-66 (personal communication from F. C. Kinsky); 113 pairs in 1966-67 (personal communication from T. S. Choate); 105 pairs in 1967-68 and 98 pairs in 1968-69 (my own work). Thus there has been a 54% decline during nine seasons. Census records of the Adelie penguin breeding population made by Choate (1967-68) and Westerskov (1968-69) indicate a decrease of a similar magnitude during the same period (personal communication from Choate and K. E. Westerskov).

The decrease in the number of skuas during and between the three seasons studied was determined from the recovery records of banded birds. During this period 95-98% of the breeding population and many non-breeding birds were marked with numbered monel-metal bands. There was no significant loss of these bands. The mean annual loss of breeding skuas was 18% compared with 6% for a stable population of skuas at Cape Crozier (personal communication from R. C. Wood). This result for the Hallett skuas probably represents a permanent loss of birds rather than sporadic return or breeding. Of the fifty breeding birds lost between 1966-67 and 1967-68, for example, only one was recovered in the 1968-69 season and as a non-breeder.

During the three seasons, twenty-three skuas, including eight breeding birds, were found dead or dying. The cause of death was established in only six cases, all resulting from human activities (wing breakages or ruptured crops caused by the

ingestion of corn cobs). No breeding birds disappeared without trace. Seasonal losses are therefore only slightly greater than might be expected for a stable population. High seasonal mortalities, however, have been recorded. In 1965-66 Kinsky recorded the deaths of thirty-three adult skuas. He analysed three of these, and discovered that they had been poisoned by ingesting parts of lead battery plates.

Figures for fledgling production (chicks fledged/females breeding) during the period of the decline are heterogeneous; 59/156 in 1959-60 (ref. 6), 116/181 in 1960-61 (ref. 7), 36/113 in 1966-67 (personal communication from Choate), 41/105 in 1967-68 and 24/98 in 1968-69 ( $\chi^2 = 21.2$ ,  $P < 0.001$ ). If, however, the 1960-61 data are removed from the calculation, no significant deviation remains ( $\chi^2 = 3.57$ ,  $P > 0.25$ ) and the resulting mean annual figure of 0.34 fledglings per breeding female compares favourably with the value of 0.33 for fledgling production at the stable Cape Crozier colony (personal communication from Wood). The high fledgling production in 1960-61 was probably, therefore, unusual, and this parameter does not seem to have changed significantly during the period of the decline. The effect of any alteration in fledgling production on the decline could, however, be recorded only after 5-6 yr, the approximate age of first breeding.

I conclude that the decline of the skua population has been a result of adults abandoning the Hallett colony as a breeding area. This decline has coincided with a period of human occupation and with the decline of the Adelie penguin population, on which skuas prey and scavenge for food. The decline in penguins has itself been established as resulting directly from human disturbance (personal communication from Choate and Westerskov). Thus although the skua decline has been an ultimate consequence of human activity, the relative importance of direct disturbance as distinct from the penguin decline as a proximate cause requires evaluation. This aspect of the study which has provided new information about the relationship between skuas and penguins will be published later.

In spite of suggestions by several workers for the elimination of possible sources of poisoning and the reduction of disturbance to both penguins and skuas, this ignominious situation has continued virtually for a decade. Holdgate<sup>3</sup> points out that, although the agreed measures for conservation under the Antarctic Treaty are comprehensive and therefore should not require significant future amendment, three areas for improvement remain, especially with regard to specially protected localities or species. These areas are the perfection of the application of the agreed measures, the development of positive schemes for management and the adoption of educational means to ensure that all personnel visiting Antarctica are aware of the need for conservation. This report should serve to endorse Holdgate's suggestions for the improvement of conservation in the Antarctic, particularly as Cape Hallett is classified as a specially protected area.

I thank Dr T. S. Choate, Mr F. C. Kinsky, Mr R. C. Wood and Dr K. E. Westerskov for valuable information.

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- <sup>1</sup> Stonehouse, B., *NZ Sci. Rev.*, **23**, 3 (1965).
- <sup>2</sup> Shimoizumi, J., *Antarctic Ecology* (edit. by Holdgate, M. W.), **2**, 946 (Academic Press, London, 1970).
- <sup>3</sup> Holdgate, M. W., *Antarctic Ecology* (edit. by Holdgate, M. W.), **2**, 924 (Academic Press, London, 1970).
- <sup>4</sup> Eklund, C. R., *Bird-Banding*, **32**, 283 (1961).
- <sup>5</sup> Reid, B. E., *Notornis*, **15**, 193 (1968).
- <sup>6</sup> Reid, B. E., *NZ DSIR Antarctic Div. Rep.* (1961).
- <sup>7</sup> Maher, W. J., *Nat. Hist.*, **75**, 42 (1966).

## Antlers—the Unbrittle Bones of Contention

In a discussion of giraffid horns and cervid antlers, Spinage<sup>1</sup> stated that the latter must be shed and regrown periodically, because bone is more brittle than horn and is often broken.

The evolution and changes in the form of antlers were undoubtedly induced by climatic and associated factors, and the annual cycle of growth, velvet removal and eventual shedding conform most strictly to the annual weather cycle in all temperate and boreal zone species<sup>2</sup>. Antlers damaged during the summer when they are soft and in velvet may continue to grow, sometimes to an aberrant final form, or growth may be arrested. In the latter event the antlers are sometimes not shed and regrown. If part of an antler is broken off during the rutting season or later, that is after the velvet has been rubbed off and the antler has hardened, no regrowth occurs but the antlers are shed as usual according to the periodicity exhibited by the species concerned. In any case, the rutting conflicts of most species are largely ritualized, antlers serving the function of display more than as jousting weapons which contact vigorously.

Perhaps less than 5% of shed antlers from caribou (*Rangifer tarandus*) and moose (*Alces alces*), for example, exhibit evidence of any breakage. When one or even two terminal tines are broken short, as occurs occasionally in Eurasian cervid species also, the mass lost is insignificant compared with that remaining. In observations of approximately a quarter of a million cervids of nine species I have recorded only one instance of breakage to the main beam itself and only two of breakage to the palm (which constitutes a large proportion of the antler mass in several species). In the former instance the beam was less than 1.5 cm in diameter and belonged to the tiny muntjac (*Muntiacus reevesi*). The losses of small parts of antler material from palms were observed in a moose and a fallow deer (*Dama dama*). Antler is less brittle than most bony material. Red deer (*Cervus elaphus*) and wapiti (*Cervus canadensis*) antlers can be flexed to some extent by hand and caribou antlers even more so. I have observed trotting bull caribou whose antlers flexed with the movement of the animal, and have observed the antlers "give" when two large bulls sparred quite gently. Collections of antlers shed by known red deer individuals indicate that breakage within an animal's lifetime may be the exception rather than the rule (personal observations and ref. 3). It is common practice among hunters in North America to eviscerate and butcher cervids, ranging from whitetail deer (*Odocoileus virginianus*) to moose, after hanging them clear of the ground by means of a mechanical hoist attached to the antlers. Because wapiti and moose may weigh up to 400 and 600 kg respectively, selection for weak and breakable antler material might operate negatively upon the eviscerator.

Considering the nutritional requirements imposed by the annual production of new and generally larger antlers, it would be an extreme over-compensation if renewal served as an allowance for possible breakage. The annual weather cycle determines the timing of antler renewal, the function and survival value of which is a consequence of the heirarchic and competitive nature of cervid behaviour<sup>2,4</sup>.

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Received December 21, 1970; revised April 4, 1971.

## Red Stained Bones from Qumran

CHEMICAL analysis of bones found in Qumran, on the Dead Sea, suggests that the members of the community of the Dead Sea Scrolls used the root of madder as a medicine to ward off evil spirits.

Bones which were stained a purplish red colour were found in seven out of ten human skeletons excavated from individual graves in the cemetery at Qumran<sup>1</sup>. Details of the bones and staining are given in Table 1.

Table 1 Bones and Staining

| Grave | Bone                    | Age * | Sex    | Position of stain                                                                                                                                                                            |
|-------|-------------------------|-------|--------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| QG 3  | Right femur             | 65    | Male   | Anterior aspect of the head to the neck                                                                                                                                                      |
| QG 4  | All teeth               | ~40   | Male   | Cavum dentis to the root                                                                                                                                                                     |
| QG 4  | Right second metacarpal | ~40   | Male   | Proximal and distal ends                                                                                                                                                                     |
| QG 5  | Left coxal bone         | 22    | Male   | Around the acetabulum and ischial tuberosity                                                                                                                                                 |
| QG 6  | Left humerus            | 25    | Female | Triangular shaped stain below the anatomical neck                                                                                                                                            |
| QG 6  | Left ulna               | 25    | Female | Posterior aspect of the olecranon                                                                                                                                                            |
| QG 9  | Right radius            | 65    | Male   | Capitulum region                                                                                                                                                                             |
| QG 10 | Left femur              | 25-26 | Male   | Diamond-shaped stain from the lesser trochanter to and including the gluteal tuberosity; an oblique line on the anterior aspect of the first third and a triangular stain above the condyles |
| QG 10 | Left humerus            | 25-26 | Male   | Entire head stained as well as a triangular stain in the deltoid insertion region                                                                                                            |
| QG 11 | Right radius            | 45-50 | Female | Upper part of the diaphysis near the bicipital tuberosity and near the distal end; greater visible dye concentration near the radial styloid process                                         |

\* Age was determined by examination of the whole skeletons.

One specimen, the right radius from grave QG 9, was sectioned to reveal the medullary cavity, which was stained throughout the length of the bone, over almost the whole surface of the cavity. Tests for the fungus *Aspergillus versicolor* proved negative, and X-ray fluorescence and atomic emission spectroscopy revealed no differences between stained and unstained bones.

During long exposure to light and air the red colour disappeared from all parts of the bones except the medullary cavities. The stain also dissipated after a few hours in contact with chloroform, acetone or ethanol, and so we needed a rapid means of determining the cause of the staining.

We dissolved the bones in dilute hydrochloric acid and obtained a red suspension which yielded a red-brown precipitate when filtered. The precipitate was washed with acetone to give a red solution from which a red residue was obtained by evaporation at reduced pressure. The infrared absorption spectrum (at 5,000-650 cm<sup>-1</sup>) of the residue, obtained by the potassium bromide pellet method, identified the stain as alizarin.

This dye, which comes from the root of the madder, *Rubia tinctorum*, was one of the most important natural dyestuffs of antiquity<sup>2</sup>. Bones of animals fed on madder become purplish-red<sup>3</sup>, and in 1736 Belchier<sup>4</sup> discovered that ingestion of madder resulted in the staining of bones *in vivo*. Since then alizarin has been used in standard laboratory practice for the

<sup>1</sup> Spinage, C. A., *Nature*, **227**, 735 (1970).

<sup>2</sup> Henshaw, J., *Nature*, **224**, 1036 (1969).

<sup>3</sup> Vogt, E., *Neue Wege der Hege* (Neumann, Neudamm, 1936).

<sup>4</sup> Geist, V., *Nature*, **220**, 813 (1968).



study of ossification<sup>4-7</sup>. The dye has a selective affinity for osteogenetic (bone forming) areas of the skeleton, where calcium salts are deposited<sup>4,8</sup> (alizarin has a chemical affinity for calcium, probably forming calcium alizarate<sup>9</sup>). Thus when growing animals are fed on madder, or injected with alizarin, the extremities of the long bones, where bone growth is most intensive, are particularly stained<sup>3</sup>.

We suggest that the bones from Qumran were stained because the community lived on a diet which included madder, which was cultivated and grew wild in the Mediterranean region, particularly around Jericho and on the shores of the Dead Sea<sup>10</sup>. The Qumran bones were stained only, or predominantly, at the extremities, and so the madder which caused the coloration must have been eaten before the completion of bone growth. The extensive red staining of the medullary cavity of the right radius of QG 9 supports the conclusion of a diet of madder; such a pattern would not be consistent with post-mortem migration of alizarin from the cloth in which the bodies might have been buried.

Madder root was made into garlands by the Jews in the Mishnaic period (second century BC to second century AD) for its supposed medical properties and as a safeguard against witchcraft<sup>11</sup>. The eating of madder root by the community of the Dead Sea Scrolls, probably to ward off illness and evil spirits, casts new light on the practices of the sect which has been identified by many scholars with the Essenes. The historian Flavius Josephus wrote that the Essenes "also take great pains in studying the writings of the ancients, and chose out of them what is most for the advantage of their soul and body; and they inquire after such roots and medicinal stones as may cure their distempers"<sup>12</sup>.

Arabs in the Middle East still attribute magical properties to madder, which they take as a sherbet drink against the "evil eye"<sup>13</sup>. The evidence that the people of Qumran also included madder in their diet points to a cultural custom which has persisted for at least two thousand years.

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- <sup>1</sup> Steckoll, S. H., *Revue de Qumran*, 6, No. 23, 325 (Paris, February 1968).
- <sup>2</sup> Hill, A. F., *Economic Botany*, second ed., 130 (McGraw-Hill, New York, 1952).
- <sup>3</sup> Le Gros Clark, W. E., *The Tissues of the Body*, fourth ed., 92, 93 (Clarendon Press, Oxford, 1958).
- <sup>4</sup> Belchier, J., *Phil. Trans.*, 39, 287, 299 (1736).
- <sup>5</sup> Cameron, G. R., *J. Path. Bact.*, 23, 929, 955 (1930).
- <sup>6</sup> Duhamel, Sur une racine qui à la faculté de teindre en rouge les os des animaux vivants; *Histoire de l'Académie Royale des Sciences—Mémoires de Mathématiques et de Physique*, 1 (1739).
- <sup>7</sup> Gottlieb, B., *Anat. Anz.*, 46, 179, 194 (1914).
- <sup>8</sup> Schour, I., Hoffman, M. M., Sarnat, B. G., and Engel, M. B., *J. Dent. Res.*, 20, 411, 418 (1941).
- <sup>9</sup> Sollmann, T., *A Manual of Pharmacology*, eighth ed., 43 (Sanders, Philadelphia, 1957).
- <sup>10</sup> Löw, I., *Die Flora der Juden*, 3, 270 (Löwitt, Vienna, 1924).
- <sup>11</sup> *Babylonian Talmud* (translation edit. by Rabbi Epstein, I.), *Shabbath*, 66b, 1, 316 (Soncino Press, London, 1958).
- <sup>12</sup> Josephus, F., *The Wars of the Jews*, Book 11, ch. 8, verse 6; *The Life and Works of Flavius Josephus* (translated by Whiston, W.), 674 (Winston, Philadelphia).
- <sup>13</sup> Salah-ed-din el Munjid, *al-Munjid fi al-lugha* (in Arabic), twentieth ed., 328, 601 (Dar el-Machreq, Beirut, 1969).

## Right and Left Handed Reading of Braille

It is generally held that in right handed people the parieto-occipital area of the left cortical hemisphere is important for the ability to read. It is also known that the right hemisphere contributes more to non-verbal, visual and spatial functions than does the left. A demonstration of this functional asymmetry was provided by Kimura<sup>1</sup>, who showed that subjects were more accurate in reporting the number of dots presented tachistoscopically the left than in the right visual field. Conversely, letters were identified better when they were presented to the right visual field; that is, the left hemisphere.

Braille reading material for the blind consists of dots in particular spatial arrangements. The question arises, therefore, whether it will be treated as other reading material, with the dominant hemisphere playing a leading part, or whether the stimuli will also be dealt with by the right hemisphere as are spatially arranged non-verbal items. Generally, teaching methods for Braille, though not rigidly applied, seem to attempt to teach a technique in which the left index finger begins, and moves up to the middle of the line, at which point the right index finger is supposed to take over, up to the end of the line. The reasons for favouring this method are not quite clear. Motoric convenience, for example, seems an inadequate explanation, in view of normal writing practice. Writing, like Braille reading, is a manual activity, but only the preferred hand is used. When we observed the reading habits of blind children, most did, in fact, use both index fingers held close together throughout each line.

In a recent investigation, fourteen blind children, aged between 8 and 10 yr, were required to read passages of Braille with either the index or centre fingers of the right or left hand. The difficulty levels of the passages were equated. The order of finger to be used, and the reading passages assigned to a particular finger, were presented according to a balanced design. Time as well as error scores were taken, and handedness was tested independently.

We found that left handed reading was significantly faster and more accurate than right handed. The effect was more marked with time ( $F=12.9$ ,  $P=0.001$ ) than with error scores ( $F=3.6$ ,  $P=0.025$ ) and more evident for centre ( $P=0.02$ ) than for index fingers ( $P=0.05$ ).

Twelve children were found to be predominantly right handed, and two seemed ambidextrous. Of these two, one read better with his right than with his left hand. The only other more efficient right handed reader was right handed. Three children, though fluent with their left hand, could not read at all with their right. These three children normally read by moving both index fingers together all along the line. Yet the left centre finger, which was not practised, was better than the right index finger.

While it could be argued that the advantage of the left over the right index finger for Braille reading may be due partly to early training and practice, this does not apply to the two centre fingers. The children stated emphatically that they normally never used these fingers for reading, yet there was a highly significant effect in favour of the left centre finger. It thus seems possible that the brain treats input such as Braille reading material as spatially arranged items, to be more efficiently analysed by the right hemisphere before or while verbal coding of the material occurs in the left.

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- <sup>1</sup> Kimura, D., *Neuropsychologia*, 4, 275 (1966).

# BOOK REVIEWS

## Pioneer of Change

*Physician to the West: Selected Writings of Daniel Drake on Science and Society.* Edited by Henry D. Shapiro and Zane L. Miller. Pp. xxxviii+419. (University of Kentucky: Lexington, June 1970.) \$12.50.

THIS is not a biography of Daniel Drake; it is a broad selection of his writings. Although it certainly appears to be a representative selection, it strives to make a point about the relationship between science and society. Daniel Drake (1785–1852) is a fascinating enough figure in his own right—physician, educator, geographer, geologist, meteorologist, entrepreneur and city planner. He reminds one of a frontier Patrick Geddes or one of the eighteenth century Scottish improvers in the breadth of his activity. The editors see him more as a representative intellectual in a particular social context than as an idiosyncratic psyche. Shapiro and Miller tend to treat the problems he addresses and the way he went about dealing with these problems as an example of the way in which the social structure may be intellectually linked to the enterprise of natural knowledge.

It is an approach which commands attention. For decades historians and sociologists of science have been grappling with the “science and society” question. One gets a feeling that the kinds of questions they have asked imply a tacit assumption about the nature of modern science—namely that “modern science” is a homogenous construct and that the kinds of social relations looked for ought to be nearly universal. Questions such as “Why did modern science arise only in the West?” “What is the relation between modern science and the economic system?” “Between modern science and religious attitudes?” This selection of Drake’s writings and the editors’ acute introductory essays prompt one to think that there are other sorts of questions about the linkage between science and the social structure which may be best addressed in a local context. For example—“What is the function of natural knowledge?” “What is the relationship between natural knowledge and social power?” These are questions worth asking and the answers to them will probably be different in different cultural and temporal contexts.

Shapiro and Miller focus on the relationship between Drake’s social

context and his problem selection and methodology. They emphasize that his work on medical topography, meteorology, geology and natural history has to be understood in the context of a developing society in the Ohio and Mississippi River Valleys. “Private” concerns—his own standing in the community of scientists on the East Coast and in Europe—were of far less importance to what Drake did than his vision of the potential contribution of natural knowledge to the social and economic development of his native region. It is wrong to separate public from private concerns in Drake’s thought. His career was a case study of the relationship of natural knowledge to social power in the context of the American frontier. One does not have to look for abstract linkages between science and society; Drake’s exertions were largely dedicated to constructing them. The scientific problems he chose were those he believed had a vital connexion with the future development of the area and he rarely had difficulty finding public platforms to expound his views. He organized literary and scientific societies, founded a major medical journal, and used his role as a medical educator to proselytize for his approach to natural knowledge and social development.

The editors characterize Drake’s approach to natural knowledge as “Baconian” and one gets the impression that this tired term has been used somewhat loosely once again. Certainly, Drake emphasized the need for observation and the collection of facts. He reacted against eighteenth century rationalism and found theorizing inappropriate on at least two counts. One was his contention that the kind of survey work immediately required for the improvement of the region necessitated a strongly inductive approach. Another was his belief that science in America was being, and ought to be, democratized. Every physician, every literate man ought to contribute to improvement by the gathering of natural observations. Science should be “for the people” in methodology as well as in aim.

Drake constantly reminded medical students that the physician had a duty both to his profession and his community. The local physician was to be the intellectual-in-residence and he ought to approach this role in the manner which would best serve profession and community. “Proceed from the known to

the unknown,” Drake advised. It was no time for theorizing; the immediate need was enlarging the sphere of the known. Drake advised future physicians to remain at home. He felt strongly that a trip to the medical centres of Europe would only accentuate a feeling of professional inferiority and remove valuable intellectuals from the frontier. Only patient attention to observation—for which local education could equip even the mediocre mind—would allow the frontier medical profession to achieve parity with European medicine. Besides—conditions in the Ohio Valley were different from conditions in Europe and studying one’s own environment was a better preparation for local medical practice than the polish of a stay in Paris or Edinburgh.

This is a well produced book and ought to be of interest to a wide variety of readers. The editors provide a comprehensive bibliography of Drake’s writings. The eighteen selections, mostly lectures, are fairly chosen and prefaced by brief notes on their significance. One does, however, feel that the 90 pages devoted to a selection from Drake’s “Natural and Statistical View . . . of Cincinnati” tell more about the environment of that town in 1815 than one really wants to know. Perhaps some of that space might have been given over to more of Drake’s response to the 1832 cholera epidemic. Charles Rosenberg, in his book on “The Cholera Years” in America, indicates that this was an episode of crucial importance to the developing social role of the American medical profession and to the relation of knowledge to medical practice. STEVEN SHAPIN

## Time Twins Again

*Time and the Space-Traveller.* By L. Marder. Pp. 210. (Allen and Unwin: London, April 1971.) £3.25.

THIS book is about the “clock paradox” and a wide range of related topics, mostly in relativity physics. After a short review of the controversies of the past two decades and a simple presentation of special relativity theory, there is a chapter on the “paradox of the twins” which presents the central theme. It has excursions into the subjects of time-perception and biological time-keeping, of accelerated clocks and the important “clock hypothesis” in relativity and even of the problem of gaining information about civilizations elsewhere in the universe.



All this is in accordance with what almost everyone, whether or not he regards them as valid, recognizes as the standard inferences from special relativity. Then there is a chapter in which Dr Marder deals in an understanding (and, in my opinion, convincing) way with the doubts and queries expressed by a number of recent critics. Marder naturally distinguishes between the question as to whether a particular result holds good in the theoretical model and as to whether something corresponding to it holds good in the world of experience; he discusses both aspects. His next chapter is, in fact, a very useful survey of the relevant experimental evidence, inevitably with special reference to the exploitation of the Mössbauer effect. The last chapter is an introduction to some basic ideas of general relativity and their bearing upon the clock paradox. Finally there is an annotated bibliography of 241 references on the clock paradox, together with many more general items.

Dr Marder confesses that "the variety of subtle and interesting points which emerged as the work progressed came as a pleasant and welcome surprise". He certainly steers a clear-minded course through them all. His book will serve readers of many classes—the general scientific reader who wants to understand what the discussion is about (without unnecessary mathematics), the teacher or student seeking material to enliven a course of relativity, the physicist interested in experimental tests of the theory, and the professional historian of science. It is an achievement

to provide for so many interests in a style that is seriously scientific but always concise and entertaining. To do this Marder has perforce to jump rather quickly from topic to topic; it is clear that he could very effectively enlarge upon certain of these topics in a further book of a rather different character and it is much to be hoped that he will do this also.

W. H. MCCREA

## Universal Mediator

*Role of Cyclic AMP in Cell Function.* Edited by Paul Greengard and Erminio Costa. (Advances in Biochemical Psychopharmacology, Vol. 3.) Pp. 386. (Raven: New York, 1970. Distributed in the Eastern Hemisphere by North-Holland, Amsterdam.) £7.35.

EVERY decade or two a metabolite appears on the biochemical scene which necessitates a reconsideration of our concepts of regulation of virtually all the major cellular functions. There is no doubt that cyclic AMP is one of these.

*The Role of Cyclic AMP in Cell Function* is the third volume in the recently launched serial publication *Advances in Biochemical Psychopharmacology* and is the outcome of a meeting held in California in February 1970. The book covers a wide area of metabolic and neurophysiological functions but, as is frequently the case with most published proceedings of conferences, the content is heterogeneous in its style, originality and interest.

The very general nature of the title is somewhat inaccurate since half of the twenty contributions concern the role of cyclic AMP in neurophysiological processes, although a serial publication on biochemical psychopharmacology would be quite justified in such a choice. It is particularly regrettable that the role of cyclic AMP in genetic transcription during catabolite repression in *Escherichia coli*, based on the elegant studies from the laboratories of Pastan, Zubay and Ullman and which leave no doubt as to the importance of this metabolic regulator throughout evolution, has been left out. One wonders whether some fundamental mechanism underlies the role of cyclic AMP in mediating the glucose effect in microorganisms as well as in mammalian tissues, intensely studied by Park and also not included. On the positive side, the book, in emphasizing the variety of neurophysiological functions dependent on cyclic AMP, succeeds in breaking the monotony of recent years concerning the involvement of this compound almost exclusively in hormone action.

The discovery of cyclic AMP by Sutherland, to whom this volume is dedicated, was the direct consequence of his work on the regulation of glycogen

metabolism by adrenaline and glucagon, "the metabolic birthplace of cyclic AMP". Over the past decade the concept of cyclic AMP as a "second messenger" in mediating the action of many, if not all, hormones has led to some unbalanced over-generalizations on how hormones work. What this book succeeds in doing, by presenting the role of cyclic AMP in the brain and its involvement in apparently non-hormonal regulations, is to show that the regulatory function of the nucleotide transcends the importance hitherto attached to this compound exclusively as a mediator of the action of some hormones.

The book begins with two very interesting and topical contributions from the laboratories of Sutherland and Rosen on the developmental acquisition of the capacity to produce or utilize cyclic AMP. Relatively little is yet known about the function of cyclic nucleotides in differentiation so that it is a pity that the recent work on identification of 'Acrasin' as cyclic AMP and its role in aggregation patterns in slime moulds is not included. A totally reliable method for the assay of cyclic AMP in biological material is yet to come and Steiner, Parker and Kipnis, in describing their novel radioimmunoassay method, have given a brief but adequate survey of the currently used methods. Greengard and Kuo stress the pivotal role of the cyclic AMP-dependent protein kinases in explaining the multiplicity of regulatory functions of the nucleotide.

The crucial identification of "phosphorylase kinase" as the site of regulation of muscle phosphorylase by E. G. Krebs's group now offers a model for further exploration. It is most appropriate therefore that Walsh, Krebs and their colleagues have discussed such a model system as well as the detection of a specific protein inhibitor of the system, although their use of the term "receptor protein" may be arguable. Langan has also presented his work on cyclic AMP-mediated phosphorylation of histones and protamines but its real significance depends upon the eventual disentanglement of the role of histones in gene transcription in higher organisms.

The four or five articles on the role of cyclic AMP in hormone action contain a pleasantly surprising amount of new information, particularly on the action of prostaglandin presented by Butcher as well as on the pineal gland by Weiss and Crayton. Rodbell's group conclude that hormones, particularly polypeptide hormones, do not act on adenyl cyclase (or at least on its catalytic site) of the target cell but, by analogy with transistor circuits and invoking the "discriminator-transducer-amplifier concept", they suggest that a

## Old Pharmacy



*Antiques of the Pharmacy.* By Leslie G. Matthews. Pp. xiv + 120. (Bell: London, June 1971.) £3.50.

separate protein or a regulatory site must be involved.

The ten chapters on brain and nerve function implicate cyclic AMP as an important regulator of a variety of processes including metabolic activity of the brain, membrane depolarization, transmission at the neuromuscular junction and synaptic functions. There is also an interesting account by Gessa *et al.* on the behavioural effects of the dibutyryl analogue of cyclic AMP injected into the brain. As regards analogues of cyclic AMP, there is virtually no discussion of cyclic GMP; this analogue is known to be metabolically active and has been identified in various tissues. These ten chapters, however, leave no doubt that we shall be hearing a great deal more in the years to come about the importance of cyclic AMP in every aspect of central nervous function, although the key to understanding the role of regulatory molecules is to a large extent dependent on the progress made in the molecular biology of the central nervous system.

Despite some of the omissions that I have pointed out, this volume on cyclic AMP is to be welcomed by all those interested in biological regulatory mechanisms, and the editors and publishers deserve our thanks for its rapid publication. It will be particularly useful to the neurobiologist but may leave some endocrinologists with a nostalgic feeling for the days when the compound was thought to be exclusively designed for hormones to work. This book, which is among the first of many to come in this field, certainly establishes cyclic AMP as an intracellular mediator of diverse metabolic processes of the same class as substances like ATP and coenzyme A.

J. R. TATA

## Life Astream

*The Ecology of Running Waters.* By H. B. N. Hynes. Pp. xxiv + 555. (Liverpool University: Liverpool, December 1970.) £7.

As the total amount of published work grows, a gap between studies of running water and the rest of limnology will inevitably open and be regretted on all grounds except those of etymology. The word "potamology" will probably come into vogue, though not as a result of any deliberate promotion by Dr Hynes, who avoids unnecessary long words and jargon. However, this, the first review of the whole field, is bound to provide a base for separate study and a separate name will be demanded.

The first three chapters deal with physical and chemical factors, the next three with attached algae, higher plants and plankton respectively. The text concludes with a chapter on the influence, generally deplorable, of man and,

before that, one on primary and secondary production and the path of energy through the ecosystem. Towards the end of the book there are four chapters on fish. The remainder of the text, about half, is devoted to invertebrates. Dr Hynes is a field naturalist with an interest in all organisms that live in running water and a curiosity about what each one does and how they all interact to produce a given type of distribution and a given community structure.

A comparatively small number of groups have invaded fresh water and have adapted their bodies and behaviour to move, respire and feed successfully in a new medium. The first step taken, further modification, has enabled some to occupy specialized niches. The rest struggle in a biotope occupied by many other species. The range of each is determined by a variety of factors, some physical and chemical, others biotic; each sperm must obtain food in competition with others while avoiding becoming food itself. Many insects have had to solve the problem of transition from water to air and back. Few adults appear to be capable of activity at winter air temperatures but, for many larvae, winter is the period of growth, possibly because there is more to eat then or because the species originated in a cold climate, or even because there is less competition or predation at that time. Total production is of academic and practical importance. In no other medium have animals to cope with a constant flow in one direction, with its advantages of a food supply brought to the door and the disadvantages of colonizing a ribbon and regaining ground after a lost foothold.

There is hardly a branch or sub-branch of biology into which an incursion has not to be made, but Dr Hynes weaves his material together skilfully to pursue a theme throughout the book. Though it remains clear that his interest is in the living organism in its environment, nothing is allowed to obtrude, and the author maintains an open-minded attitude to classifications of streams and other rigid schemes.

Data from all over the world are discussed. Sometimes the edges of a picture are blurred a little when it is illustrated by different species from different zoogeographical regions. On the other hand, workers in lands where knowledge is less advanced will be grateful that they, as well as Europeans and Americans, can find out from this book what is known.

Hynes produced a book on polluted waters in 1960 but conservationists will find the final chapter of this present one and some other parts essential reading. All concerned with ecology and production biology will find the book of value. If their interest is running water,

the book marks a watershed. Any reasonably competent review of this kind would have been welcome; that it is done by an author particularly well qualified is a bonus. Dr Hynes has had practical experience in Europe, North America and Africa. He marshals his facts in an orderly way and presents them in a clear and pleasing style. He has a good knowledge of western European languages. He also has a mother who translates papers in Russian.

T. T. MACAN

## Antibiotic Tools

*Nucleoside Antibiotics.* By R. J. Suhadolnik. Pp. x + 442. (Wiley Interscience: New York and London, January 1971.) £10.75.

RECENT years have seen a remarkable growth of interest in antibiotics as tools for biochemical research and an associated need that the mode of action should be clearly established. In this context, Dr Suhadolnik's book is a welcome addition to the literature. He arranges the nucleoside antibiotics in eleven groups. His discussion of each group begins with a short introduction and continues under the headings: discovery, production and isolation; physical and chemical properties; structure elucidation and chemical synthesis; biosynthesis; studies on growth-inhibition; and biochemical properties (usually the most extensive section). The treatment of the material is frankly aimed at understanding modes of action—there is little or no discussion of therapeutic applications. It is pleasing to learn that in several instances detailed studies at the molecular level have been carried out—the elegant work of Ward, Reich and their collaborators on *syn/anti* conformations of nucleosides, for example, in which the behaviour of formycin-containing polymers played an important part.

The book is not free from defects—there are numerous examples of proof-reading errors, for example, usually not serious. Bacteriological eyebrows may be raised at *Salutina lutea* (p. 397) and others may ask how the magical properties of heximide (p. 40) managed to escape their attention, but no one is likely to be fooled when told that the addition of the purinyl radical to culture media increases the yield of puromycin from 627 to 479 µg/ml. (p. 4). Many of the illustrations seem to have been taken directly, without re-drawing, from original publications and occasionally the reproduction is poor.

Puromycin is probably the nucleoside antibiotic with which research workers will be most familiar. One cannot envy anyone the task of disentangling the mode of action of puromycin from current ideas about the basic mechan-



isms of protein synthesis, but the author's valiant effort (pp 8-36) is not entirely successful. Nevertheless, throughout the book the bibliographies are extensive, well ordered and of great value to those wishing to gain a thorough familiarity with the field. There is an author index and a well prepared subject index.

MICHAEL WARING

## Red Light Life

*Photobiology of Micro-organisms.* Edited by Per Halldal. Pp. x+479. (Wiley Interscience: London and New York, December 1970.) £7.

THIS book is a collection of fourteen papers, each edited by an expert in the field. "Photoresponses of Fungi" is the only chapter on heterotrophic micro-organisms and most of the chapters deal with micro-algae and photosynthetic bacteria—a change to have a microbiology book where the term "microbiology" is not equated with "heterotrophic bacteria and fungi". On the whole, the approach is biological, although Duysen's introductory chapter on "Photobiological Principles and Methods" lays the physical foundation for what follows. The two chapters on the photosynthetic apparatus in algae (Halldal) and photosynthetic bacteria (Sybesma) which follow are complementary in spite of unavoidable overlap. The blue-green algae are placed firmly in the algae rather than in the photosynthetic bacteria. The chapters by Weissner on "Photometabolism of Organic Substrates" and on "Light Effects on Ion Fluxes" and Lorenzen's contribution on "Synchronous Cultures" are easily read and informative, but I found some difficulty with parts of Kowalik's chapter on "Light Effects on Carbohydrate and Protein Metabolism in Algae". Three chapters by Nultsch (photomotivation), Hand and Davenport (phototaxis and photokinesis in flagellates) and Haupt and Schönbohn (light orientated chloroplast movements) cover light dependent movement in microorganisms. Then comes Carlile's chapter on "Photoresponses of Fungi" and the final three chapters on "Photoperiodism in Micro-organisms" (a nice chapter by Dring), "Circadian Rhythms in Protozoa" (Ehret and Wille) and "Bioluminescence" (Airth *et al.*).

Collectively, the chapters provide a rounded picture of photobiology of algae and photosynthetic bacteria in the visible region. The book is well edited although there is a fair share of typographical errors and the legends to the figures require considerable tightening up. It is a pity that more room could not be found for responses in the ultra-violet such as mutagenesis, or photo-

reactivation, or photoinactivation, but an editor cannot include everything without pricing the book out of the market.

The book is fairly expensive but nevertheless a welcome addition to the field. The reference lists are excellent and comprehensive. The chapters contain a wealth of information which will be useful to graduate students and research workers on the algae and photosynthetic bacteria in particular, as well as to microbiologists in general.

W. D. P. STEWART

## Catalogue of Strata

*History of the Earth: an Introduction to Historical Geology.* By Bernhard Kummel. Second edition. Pp. xix+707. (Freeman: San Francisco and Reading, February 1971.) £5.20.

THOSE geologists who used and studied the first edition of this book will, no doubt, welcome this the second edition a decade later. The book retains the sequence and layout of its predecessor, but as so much new material, published over the last ten years, has been incorporated, it is in effect a new book. But the aims of the book are still the same—to demonstrate the purpose and methods of stratigraphy and to present a basic framework of the geological history of each of the continents.

To introduce the subject, two short chapters, on fossils and sedimentary rocks, provide much of the elementary knowledge, while brief accounts of the geological column and time scale set the subject in perspective. Each of the geological eras then receives a three-fold approach; the constituent systems in North America are described, the rocks representing the era in different countries and continents are documented and the organisms characteristic of the time period receive particular attention. The author has also included accounts of the Precambrian Shield areas and has also described the distribution, lithology and characteristic fauna of the important Gondwana Series. Such an approach covering so much ground is necessarily brief, but despite this Professor Kummel seems to have included the salient geological facts and has provided a "handbook" to world geology which is unique.

At the end of the book there are two appendices. One gives an elementary introduction to animals and plants covering mainly fundamental morphology (this is included for those readers who have insufficient exposure to zoology to cope with the palaeontology chapters, but since a preliminary knowledge of such matters is assumed throughout the book, it seems somewhat unnecessary). The second appendix consists of a set of twenty-three double-

page correlation charts, two for each of the stratigraphic systems, except the Carboniferous which has four and the Gondwana Correlation which has a single chart. In each case, one chart correlates the North American sediments and the other the rest of the world. North American stage names are inserted at the side of the "world charts" and hence a truly global correlation of the sediments is achieved, although not of course in great detail. However, their equal is not to be found in any recent textbook, and advance workers can always insert their own detail into the framework.

While the inclusion of so much basic palaeontology seems superfluous in a book of this nature, this compendium of world stratigraphy is an important addition to the literature. It provides a condensed account of many and often little-known parts of the globe, and may indeed be used as a source book for further study.

JOHN BROOKS

## Scientific Smørgasbord

*Structural Characteristics of Materials.* Edited by H. M. Finneston. (Elsevier Materials Science Series.) Pp. x+318. (Elsevier: Amsterdam, London and New York.) £8.

THIS volume belongs to the category of scientific smørgasbord. The six chapters, all by different authors, cover widely different aspects of materials science, yet have something in common; they resemble smørgasbord in that they can all with advantage be consumed together. In this they differ from a scientific journal—an expense-account meal as it were—where one paper may be prawn cocktail to the crêpes suzette of another, and the consumer needs to take his time if he is to avoid indigestion or even nausea. The only feature the two categories have in common is the rapid inflation of the price tag.

The particular volume under review resembles Swedish table in another respect: from internal evidence, most, if not all, of the chapters were written several years ago: it preserves, like pickled herring. The chapters are not necessarily the worse for this, for even today most branches of science at any given point in time advance at a fairly leisurely pace. The breakneck pace that would have been appropriate, say, to a review of pulsars a year ago is not needful when writing today on martensitic structures in steel. I have cause to know that the problems of keeping *n* authors to a deadline increase at least as *n*<sup>3</sup>; six sets of authors, however, should have been somewhat more amenable than this group appears to have been. It may be, of course, that the editor was overworked, to the extent that he has not even provided a preface

setting out the rationale of the collection.

That rationale appears to be centred on crystal structure and microstructure. The first chapter is a (necessarily) extremely superficial survey of crystallographic principles (including diffraction methods, Brillouin zones, and all sorts of goodies) in 45 pages, by H. and S. G. Lipson. It is a valiant effort, but really it represents an attempt to compress a major textbook by a factor of ten, and was doomed to failure before it began. Crocker's chapter on crystal defects covers a more restricted field and is more digestible, but in places it lays itself open to the question "so what?". There is not much on the influence of defects on properties. Hull and Roberts deal very clearly with the formal crystallography of mechanical twinning, and particularly with the factors governing choice of twinning elements. There has been much work on these factors in recent years, and many references are quoted. Within its rather narrow terms of reference this is a valuable review. Willis and Williams deal rather briefly with defects in non-stoichiometric compounds, with special reference to uranium dioxide and neutron diffraction. This is extremely specialized matter and its somewhat dated nature is revealed by the lack of any reference to the recent use of channelled bombarding ions to locate interstitial solute atoms.

The book contains two heavyweight chapters which go a long way to justify purchase: Owen and Schoen on martensitic structures and especially Nicholson and Davies on development of microstructures. The former deals remarkably clearly with the conceptually very difficult crystallography of martensitic transformations, coupled with a discussion of the nucleation and growth of martensite. There is an invaluable bibliography. The chapter on microstructures is the only one of its kind known to myself, and covers thermodynamic principles, formation of both pure and polyphase solids from the melt, and the main categories of solid-solid transformation. Always the emphasis is on the geometry of microstructures and on the energetic considerations that determine them. This chapter will be most useful introductory reading for final year undergraduates in metallurgy and materials science—and for their teachers.

During the past ten years, a large number of surveys of particular fields of materials science have been published in smørgasbord volumes: many of the references at the ends of the chapters in the volume under review are to articles in other collections. . . . Progress in This and Advances in That, the Relation Between or the Mechanism of. Many invaluable surveys lie deeply hidden in volumes such as *Progress in*

*Solid State Chemistry*, where a physical metallurgist, say, would never think of browsing, or in *Chemical and Mechanical Behaviour of Inorganic Materials* (recently reviewed in these columns). It is time for an enterprising publisher to compile a periodic Good Food Guide to Scientific Smørgasbord, perhaps in each of several categories, say Materials Science, Solid State Physics, and so on. If such a compilation could incorporate a system of grades, as does the Consumers' Association's invaluable guide to British restaurants, so much the better. At the current price of dining out, indigestion is hard to bear.

R. W. CAHN

## Plasmas Everywhere

*Solid State Plasmas.* By M. F. Hoyaux. (Applied Physics Series.) Pp. 159. (Pion: London, 1970.) £2.50 boards; £1.80 paper.

A LARGE number of moving charged particles having sufficiently high density may be defined as a plasma. Plasmas are usually considered in the liquid or gaseous phase but some of their properties are displayed by solids, more particularly conductors and semiconductors. It is the purpose of this monograph to outline the range of analogies which may be drawn, and the similarities which exist, between solid state and other plasmas. To do this, the author has written three interrelated reviews, each a condensed *Report on Progress in Physics*, emphasizing physical aspects rather than mathematical description.

An outline of solid state theory is followed by a summary of the relevant plasma physics and the two are fused in a final discussion of work on solid state plasmas. Professor Hoyaux writes with a sophistication which requires the reader to be familiar with both solid state and plasma theory if the full merit of his monograph is to be appreciated. It is a most interesting book.

An encouraging feature of physics generally and certainly of the topics outlined here is that apparent conflicts may be reconciled to the point where a common description is feasible. Both gaseous and solid state plasmas strongly resist any attempt at significant departure from charge neutrality. Both are capable of confinement by a magnetic bottle and are subject to instabilities. Collective behaviour is similar and common wave types may propagate in both media. In a gas, however, all charged particles are capable of playing an equal part while a solid state plasma is strongly degenerate with only a few electrons or holes at the Fermi surface responsible for transport phenomena.

Scattering by the solid lattice dominates its plasma properties and a wave mechanical description is necessary.

This introduces the concept of an anisotropic and varying effective mass which has no true equivalent in a gaseous plasma. Solid state plasmas have much higher densities, plasma frequencies and dielectric constants but a much lower temperature range than their gaseous counterparts.

So far the study of solid state plasmas has yielded further information on the Fermi surfaces of the solid; the future holds promise for the development of wider applications.

JOHN PAIN

## Crystallography

*Fourier Methods in Crystallography.* By G. N. Ramachandran and R. Srinivasan. (Wiley Monographs in Crystallography.) Pp. xiii + 259. (Wiley Interscience: New York and London, December 1970.) £7.50.

THIS monograph is the third of a series on various specialized aspects of crystallography. It is concerned with the problem of deriving a crystal structure by Fourier transformation of X-ray intensities, a subject with which the authors have been actively concerned for at least a decade.

The arrangement of material is very similar to that of Ramachandran's 1964 review of the same topic in *Advanced Methods of Crystallography*; new material has been added, however, and the literature coverage, which is an important part of a book of this kind, is particularly thorough. The authors begin by describing briefly the properties of Fourier transforms and go on to discuss the various ways they may be applied in diffraction studies. The Patterson function, and the image-seeking functions derived from it, are then dealt with, and the information contained in the phases illustrated by examples of phase and random syntheses. The main theme of the book is introduced by a detailed discussion of the various Fourier techniques which may be applied when part of the structure is known. Four chapters are devoted to a consideration of the best strategy to adopt with conventional heavy atom problems, and the improvement in resolution obtained by suitably weighting the Fourier coefficients is convincingly shown. The elaborations required for structure solution by the methods of isomorphous replacement and anomalous dispersion are then considered separately. Finally, Fourier techniques for applying both of these methods simultaneously are discussed.

The book is thus a compact and authoritative review of developments in structure solution by Fourier methods during the past fifteen years. It is the first survey of this topic for some time, and it should therefore prove useful to



the experienced structure analyst, particularly if his interests lie in protein crystallography. The discussion is, however, very detailed and a newcomer to the field is likely to be confused rather than enlightened.

As would be expected from the price, the book is well produced and properly indexed. There is, however, at least one serious misprint. An occasionally confusing feature is that Greek letters are sometimes written and sometimes spelt, thus gamma prime and  $\gamma'$  are used interchangeably throughout.

K. W. MUIR

## Functions for Order

*The Method of the Correlation Function in Superconductivity Theory.* By G. Lüders and K. D. Usadel. (Springer Tracts in Modern Physics, Vol. 56.) Pp. 215. (Springer-Verlag: Berlin and New York, 1971.) 78 DM; \$21.50.

THIS book is essentially a review paper covering in some detail the work initiated by Professor Dr Lüders and furthered by his collaborators at Göttingen, on certain types of second order transition from the superconducting to the normal state. This is strictly theoretical work. There is nowhere any mention of experimental results nor comparison of theory with experiment. Any reader who hopes to profit from this book must start sufficiently well versed in solid state theory that he can accept definitions like that of the function  $G$ , introduced with no more explanation than that

$$G_{\alpha\alpha'}(\mathbf{r}, \mathbf{r}') = \langle \psi_{\alpha'}^*(\mathbf{r}') \psi_{\alpha}(\mathbf{r}) \rangle$$

where "angular brackets denote an average with respect to the grand canonical ensemble" and the symbols "in the bracket are, in second quantization language, operators for the creation of an electron with spin  $\alpha'$  at the position  $\mathbf{r}'$  and for the annihilation of an electron with spin  $\alpha$  at the position  $\mathbf{r}$ ". If sentences like these are no obstacle, readers will find this a carefully written text. The authors are in general very candid: they are careful to point out where weaknesses lie; where steps in an argument, or the assumptions on which it is based are weak or where it owes a debt to other workers.

The book is divided into three parts. First comes a number of general results based ultimately on the Gorkov equations. The approach is closely modelled on one introduced by de Gennes, who showed that near a second order transition (where the pair potential  $\Delta(\mathbf{r})$  is vanishingly small), the relationship between  $\Delta(\mathbf{r})$  and the properties of normal metal can be expressed in terms of a certain correlation function, which nevertheless plays rather a minor role in the work described here.

Nevertheless, the authors say of the title they have chosen that "this baptismization (sic) should be regarded as an homage to de Gennes".

In the first part of the book, it is shown, among other things, that the problem of a superconductor in a magnetic field first taking into account boundary scattering, then scattering by impurities (magnetic and non-magnetic) can be formulated—near a second order transition at least—in terms of a distribution function obeying the Boltzmann equation. Various approximation methods are reviewed in Part II. Finally, the theory is applied in Part III to derive results for critical magnetic fields in four types of system. Some results are obtained outside the regimes of the Ginzburg-Landau and "diffusion" (short normal metal mean free path) approximations.

The English is a little eccentric in places and there is a rather large number of spelling mistakes, but neither of these things is likely to cause confusion. The frequent use of "shall" rather than "will" lends a certain flavour to the prose. To theorists interested in these problems, this will be a valuable book. It will be particularly useful to English-speaking theorists because much of the work was originally published in German. At the price, however, it is not likely to find its way to many private bookshelves.

J. G. PARK

## Soviet Telescopes

*Radio Astronomy: Instruments and Observations.* Edited by D. V. Skobel'tsyn. Translated from the Russian. (Proceedings (Trudy) of the P. M. Lebedev Physics Institute, Vol. 47.) Pp. vii+184. (Consultants Bureau: New York and London, 1971.)

TECHNICAL information on facilities for radio astronomy research in the USSR is scarce. *Lebedev Trudy 47*, originally prepared in 1968, collects together a miscellany of twenty technical reports embracing a range of subjects from heavy engineering to theoretical plasma physics. The book gives some idea of progress in instrument development up to three years ago at the Radio Astronomy Laboratory of the Lebedev Institute.

Since 1966, a group at Serpukhov has investigated how the velocity of the interplanetary plasma changes with distance from the Sun. Their instrument comprises three telescopes located at the apices of an equilateral triangle with sides 220 km in length, and simultaneous measurements at 85 MHz are made at each station. This facility is broadly similar to one built by the University of Cambridge for research on the solar wind. Unfortunately, the Soviet astronomers cannot realize the full potential of their telescope "be-

cause of the impossibility of computer analysis" for processing correlation data.

Several papers describe engineering design exercises for fully steerable parabolic reflector telescopes. One of the most difficult problems encountered in the design of large aerials is the need for high mechanical rigidity in the reflector. By supporting the reflector at many points rather than using the conventional two-point support structure, it is possible to increase the mechanical rigidity ten-fold. In the case of a 70 metre parabolic reflector, it is theoretically possible to obtain elastic distortions of only 1.2 mm (root mean square) and 3 mm (maximum). A dish constructed to these design specifications would be capable of observations at 2 cm wavelength.

In common with many other observatories, the Lebedev Institute is active in the development of low-noise parametric and maser amplifiers covering the whole gamut of radio astronomy frequencies. A typical example is a 5.2 cm spectral line receiver constructed in 1966 which has a noise temperature of 30 K.

A remarkable development is the construction of an interferometer with a 50 km baseline, operating at 34–36 MHz. Instrumental resolution has been a primary consideration in radio astronomy, and one way of achieving higher resolving power is to link widely separated telescopes by radio transmission. The first such interferometer was constructed by Jodrell Bank, and instruments in the West have usually been used for observations at frequencies of 408 MHz and higher. At 35 MHz there is a relatively high level of atmospheric and industrial interference which tends to vitiate the measurements. However, the investigation of radio source structure at lower frequencies is of great interest, and the Russian astronomers are hoping to overcome some of the interference problems by using tunable receivers which can be readjusted to select areas of low noise in the chosen waveband.

This particular version of the Russian original has fallen into a common trap. The translation was evidently not perused by an expert on the subject, so that in some parts the text reads like a computer translation: we find, for example, tract instead of waveguide, diapason for wideband and many incorrect transliterations of radio source names. All in all, the translator has spoilt the ship for a ha'p'orth of tar. The catchpenny title will doubtless trick some librarians into purchasing this book which really has very limited appeal. No observational data are presented, and most of the instrumental reports are extremely specialized.

SIMON MITTON

# CORRESPONDENCE

## Research Associations

SIR,—The difficulties of the industrial research associations and of the Government in its approach to them ("Cooperative Research in Trouble", *Nature*, 231, 206; 1971) seem to me to stem from two basic weaknesses in the original concept of a research association to serve a particular industry.

The first of these is the not-talked-about but undeniable fact that if a firm has a really good idea for a new product or process, it will strive to develop this for its own sole use and exploitation and the last body it will want to know about it is its industry RA. This is the basis of the frequent complaint by RA staffs that discussion with members is a one-way affair. Thus an RA is only likely to get a good commercial idea either from within itself or from external sources other than its own industry and is largely cut off from what should be the main source of inspiration, the industry itself.

The second weakness is seen in those RAs (most of them) whose member firms are of very different sizes. The large firm, often with scientific resources larger than that of its RA, and the small firm with few or no qualified technical staff require quite different services from the RA which may find these demands very difficult to reconcile.

A better structure for many industries would be to have a technological institute or unit associated with a particular university or polytechnic. This would provide fundamental background knowledge, act as a specialist information centre, and do such secondary but essential tasks as standards and reference work, development of test methods and so on. Such an organization would better serve the requirements of the larger companies in complementing their own technical efforts and it would also create more of the desired university-industry contacts.

The small firm would derive some benefits directly from such a centre and more indirectly but most of its needs could be met by a less-specialized but more local source of scientific advice, something like an industrial counterpart of the National Agricultural Advisory Service, though this is an unhappy analogy to draw at the present time. Possibly an expanded Industrial Liaison Officer service could fill this role.

For myself, I view with wary scepticism the present push to make the RAs commercially viable and fear that any early success they may have may be due to their living off technical capital accumulated in the previous era. Further, I think that the basic faults in their

constitution to which I have pointed will hinder them just as much in seeking sponsored research.

Yours faithfully,

ALAN JOBLING

44 Luton Road,  
Harpenden,  
Hertfordshire

## Test Ban Loophole

SIR,—Mr Scoville's letter (*Nature*, 231, 339; 1971) disputes your view that a completion of the Test Ban would "do away with the need for IAEA inspection to verify compliance with the NPT". He points out, surely rightly, that a "non-nuclear weapon nation that had unguarded fissionable material could proceed with a nuclear weapons programme without any nuclear tests" and that so far no first tests have been failures. Quite. But the IAEA safeguards on fissionable material only apply to that which is denominated "peaceful". Let the government of a non-nuclear weapon nation describe the uses to which its fissionable material is put as "military" and it escapes control. This loophole in the NPT exists to allow the construction of reactors for nuclear submarines, but the treaty's language gives blanket exclusion from control to *all* non-"peaceful" programmes.

The Soviet Union, by the way, was reported in *Le Monde* recently as offering enriched uranium to the Federal Republic of Germany merely against a minister's word that it would be used for peaceful purposes.

Yours faithfully,

MRS ELIZABETH YOUNG

100 Bayswater Road,  
London W2

## Sickle Cell Research

SIR,—The notes of your Washington correspondent (*Nature*, 231, 78; 1971) concerning research on sickle cell anaemia reflect a much publicized viewpoint, *viz.*, that the development of a practical treatment for this disease has been "curiously slow". The politically useful implication is that this has been for want of research and lack of funds. One source of this belief lies with surveys of Federal grants in which the number of projects pertinent to sickle cell disease are judged by grant title. This kind of test is akin to rating dollars for Down's syndrome without reference, for example, to studies of the mechanisms of either meiosis or aneuploidy.

Your correspondent missed a chance to set the record straight. The severity and incidence of sickle cell disease have—

for us—been well-springs of interest in haemoglobin centred research. We are not alone. For two decades the pages of *Nature* have illustrated the attention paid to haemoglobin by literally thousands of investigators. In particular, the regulation of biosynthesis and the relations between structure and function are probably better defined for haemoglobin than for any other molecule. We believe that many of these developments were prompted by the problem of sickle cell disease. We expect that the evolution of therapy for this disease will take cues from such studies. For the moment, we are conscious of the complexities encountered and it is no surprise to us that the sickling disorders cannot yet be cured. Contrary to your correspondent: the pathophysiological nature of these diseases is not well understood. We don't know how molecules of haemoglobin S aggregate; we don't know how the levels of S and the sometimes attendant—and palliative—foetal haemoglobin are controlled; we don't know whether the disease—in the United States today—really "kills half its victims before the age of 20", and we don't even know why they die.

Federal funds have been extensively and profitably used for studies of the abnormal haemoglobins and where the public has been led to believe otherwise the public has been misinformed. Our fear is that in the present clamour for delivery of medical care and in a climate of politically assigned research strategies, funds will be diverted from fundamental studies which may eventually lead to effective treatment.

Yours faithfully,

SAMUEL H. BOYER

SAMUEL CHARACHE

C. LOCKARD CONLEY

The Johns Hopkins Hospital,  
Baltimore,  
Maryland 21205

## Kill the Billion

SIR,—May I once again urge all authors to stop using the billion as a unit, and ask all editors to insist on converting billions, if authors still use them, to less ambiguous units. As a billion means  $10^{12}$  in most of Europe and only  $10^9$  in America, the possibilities of error are considerable. Those working with pesticides, where residues may occur within the range of  $10^{-6}$  and  $10^{-12}$ , are the worst offenders.

Yours faithfully,

KENNETH MELLANBY

Editor, *Environmental Pollution*,  
Monks Wood Experimental Station,  
Huntingdon



## British Diary

Monday, June 21

**Management Techniques for New Managers** (vacation school, five days) Institution of Electrical Engineers, at the University of Manchester.

Wednesday, June 23

**Interaction of Antibacterial Agents** (2 p.m.) Professor F. O'Grady, University of London, at the Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12.

## Reports and Publications

not included in the Monthly Books Supplement

### Great Britain and Ireland

Proceedings of the Royal Irish Academy. Vol. 71, Section A, No. 1: Some Covariant Identities and the Generators of the Poincaré Group. By Y. Takahashi. Pp. 1-11. 20p. Vol. 71, Section B, No. 1: The Portaskraig Tillite Succession (Dalradian) of Co. Donegal. By R. J. Howarth. Pp. 1-36+1 plate. No. 2: The Glacial Stratigraphy of the Sperrin Mountains and Its Relation to the Glacial Stratigraphy of North-West Ireland. By E. A. Colhoun. Pp. 37-52. 26p. No. 3: Late Weichselian Periglacial Phenomena of the Sperrin Mountains, Northern Ireland. By Eric A. Colhoun. Pp. 53-72 + plates 2 and 3. 32p. No. 4: Spectrophotometric Determination of Chlorate Ion in the Presence of Large Excess of Halide Ions. By P. M. Maguire and H. E. Rubalcava. Pp. 73-74. 5p. No. 5: The Age and Correlation of the Roscoe Grits, North-West Co. Galway. By D. Skevington. Pp. 75-83. 12p. (Dublin: Royal Irish Academy, 1971.) [204]

Report to the Worshipful Company of Clothworkers of the City of London of the Advisory Committee on the Departments of Textile Industries and Colour Chemistry and Dyeing in the University of Leeds for the Session 1969-1970. Pp. 72. (Leeds: The University, 1971.) [204]

Bulletin of the British Museum (Natural History). Entomology. Vol. 26, No. 1: Keys for the Identification of *Acyrtosiphon* (Hemiptera: Aphididae). By V. F. Eastop. Pp. 1-115. (London: British Museum (Natural History), 1971.) £3.40. [204]

Greenwich Time Report. Royal Greenwich Observatory. Time and Latitude Service, 1970 July-September. Pp. 153-164. (London: Science Research Council, 1970.) [204]

Natural Environment Research Council. Institute of Coastal Oceanography and Tides, 1969-1970. Pp. 28. (Birkenhead: Institute of Coastal Oceanography and Tides, 1971.) [204]

Getting the Most out of Food: The Sixth in a Series of Studies on the Modern Approach to Feeding and Nutrition. (London: Van Den Berghs and Jurgens, Ltd., 1971.) [204]

Discovery Report, Vol. XXXV, pp. 179-198: On *Ihleia magalhania* (Apstein) (Tunicata: Salpidae) and *Ihleia racovitzai* (Van Beneden). By P. Foxton. (London: Cambridge University Press, 1971.) £1.80 net; \$5. [204]

Bulletin of the British Museum (Natural History). Geology. Vol. 20, No. 2: Lower Cretaceous Ammonites from North-East England—The Hauterivian Genus *Simbirskites*. By P. F. Rawson. Pp. 25-86 + 12 plates. (London: British Museum (Natural History), 1971.) £4.30. [214]

Tropical Products Institute—Descriptive Brochure. Pp. 20. (London: Tropical Products Institute, 1971.) gratis [224]

The Zoological Society of London. Annual Report for 1970. Pp. 63. (London: The Zoological Society of London, 1971.) [224]

Proceedings of the British Ceramic Society, No. 19: Mass Transport in Non-Metallic Solids. Pp. 283. (Stoke-on-Trent: British Ceramic Society, 1971.) £4.87. [234]

Report of the Rugby School Natural History Society for the Year 1970. Pp. 23. (Rugby: Rugby School Natural History Society, 1971.) [234]

The Annual Report of the Committee of Visitors of The Royal Institution of Great Britain—The Statement of Accounts and Other Reports for the Year ending 31st December 1970. Pp. 72. (London: The Royal Institution, 1971.) [234]

PEP Broadsheet No. 526: A New Economic Mechanism?—Economic Reform in Hungary. By G. R. Denton. Pp. 30. (London: Political and Economic Planning, 1971.) 50p. [234]

### Other Countries

World Health Organization. Public Health Papers, No. 41: Mental Health of Adolescents and Young Persons—Report on a Technical Conference, Stockholm, 9-13 June 1969. By Anthony R. May, Jack H. Kahn and Börje Cronholm. Pp. 72. (Geneva: World Health Organization; London: HMSO, 1971.) 5 Sw. francs; 50p; \$1.75. [64]

The Control of Chemical and Biological Weapons. By Archibald S. Alexander *et al.* Pp. iv+130. (New York: Carnegie Endowment for International Peace, United Nations Plaza at 46th Street, 1971.) \$1. [64]

Fisheries Research Board of Canada. Technical Report No. 217: The Characterization of Petroleum Oils and their Determination in the Aquatic Environment. By V. Zitko and W. V. Carson. Pp. 29. (St. Andrews, NB: Fisheries Research Board of Canada, Biological Station, 1970.) [64]

Smithsonian Contributions to Zoology, No. 38: Copepods Parasitic on Sharks from the West Coast of Florida. By Roger F. Cressey. Pp. 30. (Washington DC: Smithsonian Institution Press, 1970. For sale by US Government Printing Office.) \$0.40. [64]

Museum of Comparative Zoology. Breviora. No. 363: Non-Specificity of Host-Selection in the Ectoparasitic Snail *Odosmoma* (*Menestho*) *Bisuturalis* (Gastropoda: Pyramidellidae). By Robert C. Bullock and Kenneth J. Boss. Pp. 7. No. 364: A New Scincid Lizard from Bougainville, Solomon Islands. By Allen E. Greer and Fred Parker. Pp. 11. No. 365: Characters and Synonymies Among the Genera of Ants. Part IV. Some Genera of Subfamily Myrmicinae (Hymenoptera: Formicidae). By William L. Brown, Jr. Pp. 5. No. 366: Pulsed Sounds of the Porpoise *Lagenorhynchus australis*. By William E. Schevill and William A. Watkins. Pp. 9. No. 367: *Micromischodius sugillatus*, a New Hemiodontid Characin Fish from Brazil, and Its Relationship to the Chilodontidae. By Tyson R. Roberts. Pp. 25. (Cambridge, Mass.: Museum of Comparative Zoology, Harvard University, 1971.) [74]

US Department of the Interior: Fish and Wildlife Service. Research Report No. 71: Review of Fishery Studies on Missouri River Main Stem Reservoirs. By Norman G. Benson. Pp. iv+61. Research Report No. 73: Predatory Behavior of Some Shore Fishes in the Gulf of California. By Edmund S. Hobson. Pp. v+92. (Washington, DC: Government Printing Office, 1968.) [74]

The Sea Otter in the Eastern Pacific Ocean. By Karl W. Kenyon. (North American Fauna, No. 68.) Pp. xiii+352. (Washington, DC: Government Printing Office, 1969.) \$1.75. [74]

Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 71-1: Report of Activities, Part A, April to October, 1970. Pp. xiii+259. (Ottawa: Queen's Printer, 1971.) \$2. [74]

US Department of the Interior: Geological Survey. Water-Supply Paper 1928: Surface Water Supply of the United States, 1961-65. Part 2: Pacific Slope Basins in California. Vol. 1: Basins from Tia Juana River to Santa Maria River. Pp. viii+501. \$2.75. Bulletin 1296: Core Logs of Three Test Holes in Cenozoic Lake Deposits Near Hector, California. By

Beth M. Madsen. Pp. iii+41. \$0.30. Professional Paper 369-B: Geohydrologic Significance of Lithofacies of the Cockfield Formation of Louisiana and Mississippi and of the Yegua Formation of Texas. By J. N. Payne. Pp. iii+14+8 plates. Professional Paper 448-A: Availability of Water in the Mississippi Embayment. By E. M. Cushing, E. H. Boswell, P. R. Speer and R. L. Hosman. Pp. v+13+7 plates. (Washington, DC: Government Printing Office, 1970.) [74]

US Department of the Interior: Bureau of Sport Fisheries and Wildlife. Propagation and Distribution of Food Fishes for the Fiscal Years 1965 and 1966. Pp. 49. North American Fauna, No. 66: Mammals of Maryland. By John L. Paradiso. Pp. iv+193. \$1. No. 65: Seven New White-Winged Doves from Mexico, Central America, and Southwestern United States. By George B. Saunders. Pp. iv+30. \$0.20. No. 67: Natural History of the King Rail. By Brooke Meanley. Pp. viii+108. \$0.60. (Washington, DC: Government Printing Office, 1968 and 1969.) [84]

Fisheries Research Board of Canada. Technical Report No. 225: Records of Associated Fauna in Scallop Dredge Hauls from the Bay of Fundy. By J. F. Caddy. Pp. 11+tables and figures. (St. Andrews, NB: Fisheries Research Board of Canada, Biological Station, 1970.) [84]

US Department of the Interior: Geological Survey. Water-Supply Paper 1981: Electrical-Analog-Model Study of Water Resources of the Columbus Area, Bartholomew County, Indiana. By F. A. Waidkin, Jr., and J. E. Heisel. Pp. iv+22+3 plates. (Washington, DC: Government Printing Office, 1970.) \$1.25. [84]

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Yale University: School of Forestry. Bulletin No. 78: Natural Variation in Susceptibility of Pinus to Neodiprion Sawflies as a Basis for the Development of a Breeding Scheme for Resistant Trees. By Walter R. Henson, Louis C. O'Neil and F. Mergen. Pp. 71. Bulletin No. 79: Chemical Analyses of Plant Tissues from the Hubbard Brook Ecosystem in New Hampshire. By G. E. Likens and F. Herbert Bormann. Pp. 25. (New Haven: Yale University, 1970.) \$2.50 each copy. [204]

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